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Science and the Open Channel

Through all ages men have tried to fathom the meaning of life. They have realized that, if some direction or meaning could be given to our actions, great human forces would be unleashed. So, many answers have been given to the question of the meaning of it all. But they have been of all different sorts, and the proponents of one answer have looked with horror at the actions of the believers in another. Horror, because from a disagreeing point of view all the great potentialities of the race were being channeled into a false and confining blind alley. In fact, it is from the history of the enormous monstrosities created by false belief that philosophers have realized the apparently infinite and wondrous capacities of human beings. The dream is to find the open channel.

What, then, is the meaning of it all? What can we say to dispel the mystery of existence? If we take everything into account, not only what the ancients knew, but all of what we know today that they did not know, then I think that we must frankly admit that *we do not know*. But, in admitting this, we have probably found the open channel.

This is not a new idea; it is the idea of the age of reason. This is the philosophy that guided the men who framed the democracy under which we live. The idea that no one really knew how to run a government led to the idea that we should arrange a system by which new ideas could be developed, tried out, rejected or retained, and more new ideas brought in —a trial-and-error system. The value of this method was realized as a result of the fact that science was already showing itself to be a successful venture at the end of the 18th century. Even then it was clear to socially minded people that the openness of the possibilities offered an opportunity, that doubt and discussion were essential for progress into the unknown. If we want to solve a problem that we have never solved before, we must leave the door to the unknown ajar.

We are at the very beginning of time for the human race. It is not unreasonable that we grapple with problems. There are tens of thousands of years in the future. Our responsibility is to do what we can, learn what we can, improve the solutions and pass them on. It is our responsibility to leave the men of the future a free hand. In the impetuous youth of humanity, we can make grave errors that can stunt our growth for a long time. This we will do if we say we have the answers now, when we are so young and ignorant; if we suppress all discussion, all criticism, saying, "This is it, boys, man is saved!" and thus doom man for a long time to the chains of authority, confined to the limits of our present imagination. It has been done so many times before.

It is our responsibility as scientists, knowing the great progress and great value of a satisfactory philosophy of ignorance, the great progress that is the fruit of freedom of thought, to proclaim the value of this freedom, to teach how doubt is not to be feared but welcomed and discussed and to defend this freedom as our duty to all coming generations.—R. P. FEYNMAN, *Norman Bridge Laboratory of Physics, California Institute of Technology.*

This editorial is based on an address, "The value of science," delivered at the autumn meeting of the National Academy of Sciences, 2 to 4 Nov. 1955; the address was published in Engineering and Science *(1 Dec. 1955) and is used here by permission.*

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On the Origin of Cancer Cells

Otto Warburg

Our principal experimental object for the measurement of the metabolism of cancer cells is today no longer the tumor but the ascites cancer cells (*1*) living free in the abdominal cavity, which are almost pure cultures of cancer cells with which one can work quantitatively as in chemical analysis. Formerly, it could be said of tumors, with their varying cancer cell content, that they ferment more strongly the more cancer cells they contain, but today we can determine the absolute fermentation values of the cancer cells and find such high values that we come very close to the fermentation values of wildly proliferating *Torula* yeasts.

What was formerly only qualitative has now become quantitative. What was formerly only probable has now become certain. The era in which the fermentation of the cancer cells or its importance could be disputed is over, and no one today can doubt that we understand the origin of cancer cells if we know how their large fermentation originates, or, to express it more fully, if we know how the damaged respiration and the excessive fermentation of the cancer cells originate.

Energy of Respiration and Fermentation

We now understand the chemical mechanism of respiration and fermentation almost completely, but we do not need this knowledge for what follows, since *energy alone* will be the center of our considerations. We need to know no more of respiration and fermentation here than that they are energy-producing reactions and that they synthesize the energy-rich adenosine triphosphate, through which the energy of respiration and fermentation is then made available for life. Since it is known how much adenosine triphosphate can be synthesized by respiration and how much by fermentation, we can write immediately the potential, biologically utilizable energy production of any cells if we have measured their respiration and fermentation. With the ascites cancer cells of the mouse, for example, we find an average respiration of 7 cubic millimeters of oxygen consumed per milligram, per hour, and fermentation of 60 cubic millimeters of lactic acid produced per milligram, per hour. This, converted to energy equivalents, means that the cancer cells can obtain approximately the same amount of energy from fermentation as from respiration, whereas the normal body cells obtain much more energy from respiration than from fermentation. For example, the liver and kidney of an adult animal obtain about 100 times as much energy from respiration as from fermentation.

I shall not consider aerobic fermentation, which is a result of the interaction of respiration and fermentation, because aerobic fermentation is too labile and too dependent on external conditions. Of importance for the considerations that follow are only the two stable independent metabolic processes, respiration and *anaerobic* fermentation—respiration, which is measured by the oxygen consumption of cells that are saturated with oxygen, and fermentation, which is measured by the formation of lactic acid in the absence of oxygen.

Injuring of Respiration

Since the respiration of all cancer cells is damaged, our first question is, How can the respiration of body cells be injured? Of this damage to respiration, it can be said at the outset that it must be *irreversible*, since the respiration of cancer cells never returns to normal. Second, the injury to respiration must not be so great that the cells are killed, for then no cancer cells could result. If respiration is damaged when it forms too little adenosine triphosphate, it may be either that the oxygen consumption has been decreased or that, with undiminished oxygen consumption, the coupling between respiration and the formation of adenosine triphosphate has been broken, as was first pointed out by Feodor Lynen (*2*).

One method for the destruction of the respiration of body cells is removal of oxygen. If, for example, embryonal tissue is exposed to an oxygen deficiency for some hours and then is placed in oxygen again, 50 percent or more of the respiration is usually destroyed. The cause of this destruction of respiration is lack of energy. As a matter of fact, the cells need their respiratory energy to preserve their structure, and if respiration is inhibited, both structure and respiration disappear.

Another method for destroying respiration is to use respiratory poisons. From the standpoint of energy, this method comes to the same result as the first method. No matter whether oxygen is withdrawn from the cell or whether the oxygen is prevented from reacting by a poison, the result is the same in both cases—namely, impairment of respiration from lack of energy.

I may mention a few respiratory poisons. A strong, specific respiratory poison is arsenious acid, which, as every clinician knows, may produce cancer. Hydrogen sulfide and many of its deriv-

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Professor Warburg is director of the Max Planck Institute for Cell Physiology, Berlin-Dahlem, Germany. This article is based on a lecture delivered at Stuttgart on 25 May 1955 before the German Central Committee for Cancer Control. It was first published in German [*Naturwissenschaften* 42, 401 (1955)]. This translation was prepared by Dean Burk, Jehu Hunter, and W. H. Everhardy of the U.S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, Bethesda, Md., with the permission of *Naturwissenschaften* and with the collaboration of Professor Warburg, who has introduced additional material.

atives are also strong, specific respiratory poisons. We know today that certain hydrogen sulfide derivatives, thiourea and thioacetamide, with which citrus fruit juices have been preserved in recent times, induce cancer of the liver and gall bladder in rats.

Urethane is a nonspecific respiratory poison. It inhibits respiration as a chemically indifferent narcotic, since it displaces metabolites from cell structures. In recent years it has been recognized that subnarcotic doses of urethane cause lung cancer in mice in 100 percent of treatments. Urethane is particularly suitable as a carcinogen, because, in contrast to alcohol, it is not itself burned up on the respiring surfaces and, unlike ether or chloroform, it does not cytolyze the cells. Any narcotic that has these properties may cause cancer upon chronic administration in small doses.

The first notable experimental induction of cancer by oxygen deficiency was described by Goldblatt and Cameron (*3*), who exposed heart fibroblasts in tissue culture to intermittent oxygen deficiency for long periods and finally obtained transplantable cancer cells, whereas in the control cultures that were maintained without oxygen deficiency, no cancer cells resulted. Clinical experiences along these lines are innumerable: the production of cancer by intermittent irritation of the outer skin and of the mucosa of internal organs, by the plugging of excretory ducts of glands, by cirrhoses of tissues, and so forth. In all these cases, the intermittent irritations lead to intermittent circulatory disturbances. Probably chronic intermittent oxygen deficiency plays a greater role in the formation of cancer in the body than does the chronic administration of respiratory poisons.

Any respiratory injury due to lack of energy, however, whether it is produced by oxygen deficiency or by respiratory poisons, must be cumulative, since it is irreversible. Frequent small doses of respiratory poisons are therefore more dangerous than a single large dose, where there is always the chance that the cells will be killed rather than that they will become carcinogenic.

Grana

If an injury of respiration is to produce cancer, this injury must, as already mentioned, be irreversible. We understand by this not only that the inhibition of respiration remains after removal of the respiratory poison but, even more, that the inhibition of respiration also continues through all the following cell divisions, for measurements of metabolism in transplanted tumors have shown that cancer cells cannot regain normal respiration, even in the course of many decades, once they have lost it.

This originally mysterious phenomenon has been explained by a discovery that comes from the early years of cell physiology (*4*). When liver cells were cytolyzed by infusion of water and the cytolyzate was centrifuged, it was found that the greater part of the respiration sank to the bottom with the cell grana. It was also shown that the respiration of the centrifuged grana was inhibited by narcotics at concentrations affecting cell structures, from which it was concluded —already in 1914—that the respiring grana are not insoluble cell particles but *autonomous organisms,* a result that has been extended in recent years by the English botanist Darlington (*5*) and particularly by Mark Woods and H. G. du Buy (*6*) of the National Cancer Institute in Bethesda, Md. Woods and du Buy have experimentally expanded our concepts concerning the self-perpetuating nature of mitochondrial elements (grana) and have demonstrated the hereditary role of extranuclear aberrant forms of these in the causation of neoplasia. The autonomy of the respiring grana, both biochemically and genetically, can hardly be doubted today.

If the principle *Omne granum e grano* is valid for the respiring grana, we understand why the respiration connected with the grana remains damaged when it has once been damaged; it is for the same reason that properties linked with genes remain damaged when the genes have been damaged.

Furthermore, the connection of respiration with the grana (*7*) also explains a carcinogenesis that I have not mentioned previously, the carcinogenesis by x-rays. Rajewsky and Pauly have recently shown that the respiration linked with the grana can be destroyed with strong doses of x-rays, while the small part of the respiration that takes place in the fluid protoplasm can be inhibited very little by irradiation. Carcinogenesis by x-rays is obviously nothing else than a destruction of respiration by elimination of the respiring grana.

It should also be mentioned here that grana, as Graffi has shown (*8*), fluoresce brightly if carcinogenic hydrocarbons are brought into their surroundings, because the grana accumulate the carcinogenic substances. Probably this accumulation is the explanation for the fact that carcinogenic hydrocarbons, although almost insoluble in water, can inhibit respiration and therefore have a carcinogenic effect.

Increase of Fermentation

When the respiration of body cells has been irreversibly damaged, cancer cells by no means immediately result. For cancer formation there is necessary not only an irreversible damaging of the respiration but also an increase in the fermentation—indeed, such an increase of the fermentation that the failure of respiration is compensated for energetically. But how does this increase of fermentation come about?

The most important fact in this field is that there is no physical or chemical agent with which the fermentation of cells in the body can be increased directly; for increasing fermentation, a long time and many cell divisions are always necessary. The temporal course of this increase of fermentation in carcinogenesis has been measured in many interesting works, among which I should like to make special mention of those of Dean Burk (*9*).

Burk first cut out part of the liver of healthy rats and investigated the metabolism of the liver cells in the course of the ensuing regeneration, in which, as is well known, the liver grows more rapidly than a rapidly growing tumor. No increase of fermentation was found. Burk then fed rats for 200 days on butter yellow, whereupon liver carcinomas were produced, and he found that the fermentation slowly increased in the course of 200 days toward values characteristic of tumors.

The mysterious latency period of the production of cancer is, therefore, nothing more than the time in which the fermentation increases after a damaging of the respiration. This time differs in various animals; it is especially long in man and here often amounts to several decades, as can be determined in the cases in which the time of the respiratory damage is known—for example, in arsenic cancer and irradiation cancer.

The driving force of the increase of fermentation, however, is the energy deficiency under which the cells operate after destruction of their respiration, which forces the cells to replace the irretrievably lost respiration energy in some way. They are able to do this by a selective process that makes use of the fermentation of the normal body cells. The more weakly fermenting body cells perish, but the more strongly fermenting ones remain alive, and this selective process continues until the respiratory failure is compensated for energetically by the increase in fermentation. Only then has a cancer cell resulted from the normal body cell.

Now we understand why the increase in fermentation takes such a long time and why it is possible only with the help of many cell divisions. We also understand why the latency period is different in rats and in man. Since the average fermentation of normal rat cells is much greater than the average fermentation

of normal human cells, the selective process begins at a higher fermentation level in the rat and, hence, is completed more quickly than it is in man.

It follows from this that there would be no cancers if there were no fermentation of normal body cells, and hence we should like to know, naturally, from where the fermentation of the normal body cells stems and what its significance is in the body. Since, as Burk has shown, the fermentation remains almost zero in the regenerating liver growth, we must conclude that the fermentation of the body cells has nothing to do with normal growth. On the other hand, we have found that the fermentation of the body cells is greatest in the very earliest stages of embryonal development and that it then decreases gradually in the course of embryonal development. Under these conditions, it is obvious—since ontogeny is the repetition of phylogeny—that the fermentation of body cells is the inheritance of undifferentiated ancestors that have lived in the past at the expense of fermentation energy.

Structure and Energy

But why—and this is our last question—are the body cells dedifferentiated when their respiration energy is replaced by fermentation energy? At first, one would think that it is immaterial to the cells whether they obtain their energy from respiration or from fermentation, since the energy of both reactions is transformed into the energy of adenosine triphosphate, and yet adenosine triphosphate = adenosine triphosphate. This equation is certainly correct chemically and energetically, but it is incorrect morphologically, because, although respiration takes place for the most part in the structure of the grana, the fermentation enzymes are found for a greater part in the fluid protoplasm. The adenosine triphosphate synthesized by respiration therefore involves more structure than the adenosine triphosphate synthesized by fermentation. Thus, it is as if one reduced the same amount of silver on a photographic plate by the same amount of light, but in one case with diffused light and in the other with patterned light. In the first case, a diffuse blackening appears on the plate, but in the second case, a picture appears; however, the same thing happens chemically and energetically in both cases. Just as the one type of light energy involves more structure than the other type, the adenosine triphosphate energy involves more structure when it is formed by respiration than it does when it is formed by fermentation.

In any event, it is one of the fundamental facts of present-day biochemistry that adenosine triphosphate can be synthesized in homogeneous solutions with crystallized fermentation enzymes, whereas so far no one has succeeded in synthesizing adenosine triphosphate in homogeneous solutions with dissolved respiratory enzymes, and the structure always goes with oxidative phosphorylation.

Moreover, it was known for a long time before the advent of crystallized fermentation enzymes and oxidative phosphorylation that fermentation—the energy-supplying reaction of the lower organisms—is morphologically inferior to respiration. Not even yeast, which is one of the lowest forms of life, can maintain its structure permanently by fermentation alone; it degenerates to bizarre forms. However, as Pasteur showed, it is rejuvenated in a wonderful manner if it comes in contact with oxygen for a short time. "I should not be surprised," Pasteur said in 1876 (*10*) in the description of these experiments, "if there should arise in the mind of an attentive hearer a presentiment about the causes of those great mysteries of life which we conceal under the words youth and age of cells." Today, after 80 years, the explanation is as follows: the firmer connection of respiration with structure and the looser connection of fermentation with structure.

This, therefore, is the physicochemical explanation of the dedifferentiation of cancer cells. If the structure of yeast cannot be maintained by fermentation alone, one need not wonder that highly differentiated body cells lose their differentiation upon continuous replacement of their respiration with fermentation.

I would like at this point to draw attention to a consequence of practical importance. When one irradiates a tissue that contains cancer cells as well as normal cells, the respiration of the cancer cells, already too small, will decline further. If the respiration falls below a certain minimum that the cells need unconditionally, despite their increased fermentation, they die; whereas the normal cells, where respiration may be harmed by the same amount, will survive because, with a greater initial respiration, they will still possess a higher residual respiration after irradiation. This explains the selective killing action of x-rays on cancer cells. But still further: the descendants of the surviving normal cells may in the course of the latent period compensate the respiration decrease by fermentation increase and, thence, become cancer cells. Thus it happens that radiation which kills cancer cells can also at the same time produce cancer or that urethane, which kills cancer cells, can also at the same time produce cancer. Both events take place from harming respiration: the killing, by harming an *already* harmed respiration; the carcinogenesis by the harming of a *not yet* harmed respiration.

Maintenance Energy

When dedifferentiation of the body cells has occurred and cancer cells have thereby developed, there appears a phenomenon to which our attention has been called by the special living conditions of the ascites cancer cells. In extensively progressed ascites cancer of the mouse, the abdominal cavity contains so many cancer cells that the latter cannot utilize their full capacity to respire and ferment because of the lack of oxygen and sugar. Nevertheless, the cancer cells remain alive in the abdominal cavity, as the result of transplantation proves.

Recently we have confirmed this result by direct experiments in which we placed varying amounts of energy at the disposal of the ascites outside the body, *in vitro*, and then transplanted it. This investigation showed that all cancer cells were killed when no energy at all was supplied for 24 hours at 38°C but that one-fifth of the growth energy was sufficient to preserve the transplantability of the ascites. This result can also be expressed by saying that cancer cells require much less energy to keep them alive than they do for growth. In this they resemble other lower cells, such as yeast cells, which remain alive for a long time in densely packed packets—almost without respiration and fermentation.

In any case, the ability of cancer cells to survive with little energy, if they are not growing, will be of great importance for the behavior of the cancer cells in the body.

Sleeping Cancer Cells

Since the increase in fermentation in the development of cancer cells takes place gradually, there must be a transitional phase between normal body cells and fully formed cancer cells. Thus, for example, when fermentation has become so great that dedifferentiation has commenced, but not so great that the respiratory defect has been fully compensated for energetically by fermentation, we may have cells which indeed look like cancer cells but are still energetically insufficient. Such cells, which are clinically not cancer cells, have lately been found, not only in the prostate, but also in the lungs, kidney, and stomach of elderly persons. Such cells have been referred to as "sleeping cancer cells" (*11*, *12*).

The sleeping cancer cells will possibly play a role in chemotherapy. From energy considerations, I could think that

sleeping cancer cells could be killed more readily than growing cancer cells in the body and that the most suitable test objects for finding effective killing agents would be the sleeping cancer cells of skin—that is, precancerous skin.

Summary

Cancer cells originate from normal body cells in *two* phases. The first phase is the irreversible injuring of respiration. Just as there are many remote causes of plague—heat, insects, rats—but only one common cause, the plague bacillus, there are a great many remote causes of cancer—tar, rays, arsenic, pressure, urethane—but there is only one common cause into which all other causes of cancer merge, the irreversible injuring of respiration.

The irreversible injuring of respiration is followed, as the second phase of cancer formation, by a long struggle for existence by the injured cells to maintain their structure, in which a part of the cells perish from lack of energy, while another part succeed in replacing the irretrievably lost respiration energy by fermentation energy. Because of the morphological inferiority of fermentation energy, the highly differentiated body cells are converted by this into undifferentiated cells that grow wildly—the cancer cells.

To the thousands of quantitative experiments on which these results are based, I should like to add, as a further argument, the fact that there is no alternative today. If the explanation of a vital process is its reduction to physics and chemistry, there is today no other explanation for the origin of cancer cells, either special or general. From this point of view, *mutation* and *carcinogenic agent* are not alternatives, but empty words, unless metabolically specified. Even more harmful in the struggle against cancer can be the continual discovery of miscellaneous cancer agents and cancer viruses, which, by obscuring the underlying phenomena, may hinder necessary preventive measures and thereby become responsible for cancer cases.

Technical Considerations and Comments

Metabolism of the ascites cancer cells. The high fermentation of ascites cancer cells was discovered in Dahlem in 1951 (*12*) and since then has been confirmed in many works (*13, 14*). For best measurements, the ascites cells are not transferred to Ringer's solution but are maintained in their natural medium, ascites serum, which is adjusted physiologically at the beginning of the measurement by addition of glucose and bicarbonate. Because of the very large fermentation, it is necessary to dilute the ascites cells that are removed from the abdominal cavity rather considerably with ascites serum; otherwise the bicarbonate would be used up within a few minutes after addition of the glucose, and hence the fermentation would be brought to a standstill.

Under physiological conditions of *p*H and temperature, we find the following metabolic quotients in ascites serum (*15*):

$$Q_{O_2} = -5 \text{ to } -10$$

$$Q_M^{O_2} = 25 \text{ to } 35$$

$$Q_M^{N_2} = 50 \text{ to } 70$$

where Q_{O_2} is the amount of oxygen in cubic millimeters that 1 milligram of tissue (dry weight) consumes per hour at 38°C with oxygen saturation, $Q_M^{O_2}$ is the amount of lactic acid in cubic millimeters that 1 milligram of tissue (dry weight) develops per hour at 38°C with oxygen saturation, and $Q_M^{N_2}$ is the amount of lactic acid in cubic millimeters that 1 milligram of tissue (dry weight) develops per hour at 38°C in the absence of oxygen.

Even higher fermentation quotients have been found in the United States with other strains of mouse ascites cancer cells (*13, 14*).

All calculations of the energy-production potential of cancer cells should now be based on the quotients of the ascites cancer cells, since these quotients are 2 or 3 times as large anaerobically as the values formerly found for the purest solid tumors. The quotients of the normal body cells, however, remain as they were found in Dahlem in the years from 1924 to 1929 (*16–19*). It is clear that the difference in metabolism between normal cells and cancer cells is much greater than it formerly appeared to be on the basis of measurements on solid tumors.

Utilizable energy of respiration and fermentation. Since the discovery of the oxidation reaction of fermentation in 1939 (*20*), we have known the chemical reactions by which adenosine diphosphate is phosphorylated to adenosine triphosphate in fermentation; and since then we have found that 1 mole of fermentation lactic acid produces 1 mole of adenosine triphosphate (ATP).

The chemical reactions by which ATP is synthesized in respiration are still unknown, but it can be assumed, according to the existing measurements (*21*), that 7 moles of ATP can be formed when 1 mole of oxygen is consumed in respiration.

ATP quotients. If we multiply Q_{O_2} by 7 and $Q_M^{N_2}$ by 1, we obtain the number of cubic millimeters of ATP that 1 milligram of tissue (dry substance) can synthesize per hour (22,400 cubic millimeters = 1 millimole of ATP). We call these quotients $Q_{ATP}^{O_2}$ and $Q_{ATP}^{N_2}$, according to whether the ATP is formed by respiration or by fermentation, respectively.

Energy production of cancer cells and of normal body cells. In Table 1, the Q values of some normal body cells are contrasted with the Q values of our ascites cancer cells.

The cancer cells have about as much energy available as the normal body cells, but the ratio of the fermentation energy to the respiration energy is much greater in the cancer cells than it is in the normal cells.

Uncoupling of respiration. If a young rat embryo is transferred from the amniotic sac to Ringer's solution, the previously transparent embryo becomes opaque and soon appears coagulated (*17*). At the same time, the connection between respiration and phosphorylation is broken; that is, although oxygen is still consumed and carbon dioxide is still developed, the energy of this combustion process is lost for life. If the metabolism quotients had previously been

$$Q_{O_2} = -15,\ Q_M^{O_2} = 0,\ Q_M^{N_2} = 25,$$
$$Q_{ATP}^{O_2} = 105,\ Q_{ATP}^{N_2} = 25$$

in the amniotic fluid, afterward, in Ringer's solution, they are

$$Q_{O_2} = -15,\ Q_M^{O_2} = 25,\ Q_M^{N_2} = 25,$$
$$Q_{ATP}^{O_2} = 0,\ Q_{ATP}^{N_2} = 25$$

Because of uncoupling of respiration and phosphorylation, the energy production of the embryo has fallen from $Q_{ATP}^{O_2} + Q_{ATP}^{N_2} = 130$, to 25; since the uncoupling is irreversible, the embryo dies in the Ringer's solution.

This example will show that the first phase of carcinogenesis, the irreversible damaging of respiration, need not be an actual decrease in the respiration quotient but merely an uncoupling of respiration, with undiminished over-all oxygen consumption. Ascites cancer cells, which owe their origin primarily to an uncoupling of respiration, could conceivably have the following metabolism quotients, for example:

$$Q_{O_2} = -50,\ Q_M^{O_2} = 100,\ Q_M^{N_2} = 100,$$
$$Q_{ATP}^{O_2} = 0,\ Q_{ATP}^{N_2} = 100$$

which would mean that, despite great respiration, the usable energy production would be displaced completely toward the side of fermentation. One will now have to search for such cancer cells among the ascites cancer cells. Solid tumors—and especially solid spontaneous tumors—need no longer be subjected to such examinations today, of course, since the solid tumors are usually so impure histologically.

Aerobic fermentation. Aerobic fermentation is a property of all growing cancer cells, but aerobic fermentation

without growth is a property of damaged body cells—for example, embryos that have been transferred from amniotic fluid to Ringer's solution. Since it is always easy to detect aerobic fermentation but generally difficult to detect growth, or lack thereof, of body cells, aerobic fermentation should not be used as a test for cancer cells, as I made clear in 1928 (*19*).

Nevertheless, misuse is still made of aerobic fermentation. Thus, O'Connor (*22*) recently repeated our old experiments on the aerobic fermentation of the embryo that has been transferred into Ringer's solution, but he drew the conclusion that the growth of normal body cells is completed at the expense of the aerobic fermentation, even though it has long been established that the embryo does not ferment aerobically when it grows in the amniotic fluid.

Respiratory poisons. The specific respiration-inhibiting effect of arsenious acid and the irreversibility of its inhibitions were discovered in the first quantitative works on cell respiration (*23, 24*). There is abundant literature on the carcinogenesis by arsenic, particularly on arsenic cancer after treatment of psoriasis and on the cancer of grape owners who spray their vineyards with arsenic. The specific respiration-inhibiting effect of hydrogen sulfide has likewise been described by Negelein (*25*), and carcinogenesis by derivatives of hydrogen sulfide has been recently described by D. N. Gupta (*26*).

The irreversible inhibition of cell respiration by urethane was discovered early (*27*) as well as the fact that the urethane inhibition is more irreversible the higher the temperature. In sea urchin eggs, the effect of urethane was investigated, not only on the metabolism, but also on cell division in studies (*28*) from which the later urethane treatment of leukemia was developed. The physicochemical mechanism by which urethane and other indifferent narcotics inhibit cell respiration was cleared up in 1921 (*29*). Only much later did the carcinogenic effect of urethane become known. Actually, multiple lung adenomas can often be produced in 100 percent of the mice treated with small doses of urethane (*30*).

Oxygen deficiency. Short-period oxygen deficiency irreversibly destroys the respiration of embryos (*16*) without thereby inhibiting the anaerobic fermentation of the embryo. If such embryos are transplanted, teratomas are formed (*31*). It has recently been reported that, in the development of the Alpine salamander, malformations occurred when the respiration was inhibited by hydrocyanic acid in the early stages of embryonal development (*32*).

Goldblatt and Cameron (*3*) reported that, in the *in vitro* culturing of fibroblasts, tumor cells appeared when the cultures were exposed to intermittent oxygen deficiency for long periods, whereas, in the control cultures, no tumor cells appeared. In the discussion at the Stuttgart convention, Lettré cited against Goldblatt and Cameron the fact that another American tissue culturist, Earle, has occasionally obtained tumor cells from fibroblasts for reasons unknown to him and in an unreproduceable manner, but this objection does not seem weighty, and the latter part is untrue (*33*). In any event, here is an area in which the methods of tissue culture could prove useful for cancer research. But warnings must be given against metabolism measurements in tissue cultures, if and when the tissue cultures are mixtures of growing and dying cells, especially under conditions of malnutrition. An example of the latter type of confusion is involved in the discussion by Albert Fischer (*34*), especially in the chapter "Energy exchange of tissue cells cultivated *in vitro*."

Rous agent. If the Rous agent is inoculated into the chorion of chick embryos, tumors originate in the course of a few days—as rapidly as in the transplantation of cancer cells. The tumors formed are not chorion tumors but Rous sarcomas. The Rous agent, to which a particle weight of 150 million is ascribed at present, is therefore capable of transmitting the morphological properties of the Rous sarcoma; and whatever we call the Rous agent—"hereditary unit," cell fragment, microcell, or spore—the transmission of the Rous sarcoma by the Rous agent is, in any case, nothing more than a *transplantation* and is to be differentiated strictly from the production of a chicken sarcoma by methylcholanthrene, which is a *neoformation* of a tumor from normal body cells and as such takes a long time.

The metabolism of the chicken sarcomas, whether produced by the Rous agent or by methylcholanthrene, is the same and does not differ in any way from the metabolism of the tumors of other animals (*35*). In the first case, however, the fermentation potential has been transplanted with the Rous agent, whereas in the second case the fermentation has been intensified by selection from normal body cells under the action of the methylcholanthrene.

Table 1. Contrast of the Q values of some normal body cells with the Q values of ascites cancer cells.

Cells	Q_{O_2}	$Q_{M}^{N_2}$	$Q_{ATP}^{O_2}$	$Q_{ATP}^{N_2}$	$Q_{ATP}^{O_2} + Q_{ATP}^{N_2}$
Liver	−15	1	105	1	106
Kidney	−15	1	105	1	106
Embryo (very young)	−15	25	105	25	130
Cancer	− 7	60	49	60	109

Addendum: in vitro Carcinogenesis and Metabolism

Since this paper was prepared, striking confirmation and extension of its main conclusions have been obtained from correlated metabolic and growth studies of two lines of tissue culture cancer cells of widely differing malignancy that were both derived from *one and the same* normal, tissue-culture cell (*36*). The single cell was isolated some 5 years ago from a 97-day old parent culture of normal subcutaneous adipose tissue of a strain C3H/He mouse by Sanford, Likely, and Earle (*33*) of the National Cancer Institute. Up to the time that the single-cell isolation was made, no tumors developed when cells of the parent culture were injected into strain C3H/He mice. Injections of *in vitro* cells of the lines 1742 and 2049 (formerly labeled substrains VII and III, respectively) first produced tumors in normal C3H/He mice after the 12th and 19th *in vitro* transplant generations, respectively; after 1½ years, the percentage production of sarcomas was 63 and 0 percent, respectively; and after 3 years, it was 97 and 1 percent, respectively, with correspondingly marked differences in length of induction period. Despite such gross differences in "malignancy" *in vivo*, the rates of growth of the two lines of cells maintained continuously *in vitro* have remained nearly identical and relatively rapid. Nevertheless, the metabolism of the two lines of cancer cells, whose malignancy was developed *in vitro*, has been found by Woods, Hunter, Hobby, and Burk to parallel strikingly the differences in malignancy observed *in vivo*, in a manner in harmony with the predications and predictions of this article.

The metabolic values were measured following direct transfer of the liquid cultures from the growth flasks into manometric vessels, without notable alteration of environmental temperature, *p*H, or medium composition (horse serum, chick embryo extract, glucose, bicarbonate, balanced saline). The values obtained thus accurately represent the metabolism of growing, adequately nourished, pure lines of healthy cancer cells free of admixture with any other tissue cell type. The anaerobic glycolysis of the high-malignancy line 1742 was $Q_{M}^{N_2} = 60$ to 80, which is virtually max-

imum for any and all cancer cells previously reported, including ascites cells (*12–14*). The anaerobic glycolysis of the low-malignancy line was, however, only one-third as great, $Q_M{}^{N_2} = 20$ to 30. The average aerobic glycolysis values for the two lines were in the same order, $Q_M{}^{O_2} =$ 30 and 10, respectively, but of lower magnitude because of the usual, pronounced Pasteur effect, greater in line 1742 than in line 2049 ($Q_M{}^{N_2} - Q_M{}^{O_2} =$ about 40 and 15). On the other hand, the rates of oxygen consumption were in the converse order, being smaller in line 1742 ($Q_{O_2} = 5$ to 10) than in line 2049 ($Q_{O_2} = 10$ to 15), corresponding to a greater degree of respiratory defect in line 1742. The respiratory defect in both lines was further delineated by the finding of little or no increase in respiration after the addition of succinate to either line of cells, in contrast to the considerable increases obtained with virtually all normal tissues (*9*); and the respiratory increase with paraphenylenediamine was likewise relatively low, compared with normal tissue responses.

A further notable difference between the two cell lines was the very much lower inhibition of glycolysis by podophyllin materials (anti-insulin potentiators) observed with line 1742 compared with line 2049 (for example, 10 and 70 percent, respectively, at a suitably low concentration). This result would be expected on the basis of the much greater loss of anti-insulin hormonal restraint of glucose metabolism, at the hexokinase phosphorylating level, as the degree of malignancy is increased, just as was reported for a spectrum of solid tumors (*14*).

Finally, the high-malignancy line 1742 cells have been found by A. L. Schade to contain 3 times as much aldolase as the low-malignancy line 2049 cells (11,300 versus 3700 Warburg activity units per milliliter of packed cells extracted), and about 2 times as much α-glycerophosphate dehydrogenase [2600 versus 1400 Schade activity units (*13*) per milliliter of packed cells extracted]. The potential significance of these indicated enzymic differences in relation to the parallel glycolytic differences, measured with aliquots of the same cell cultures, is evident, and may well be connected with the corresponding hexokinase system differences.

The new metabolic data on the two remarkably contrasting lines of cancer cells, which originated from a single, individual cell and have been maintained exclusively *in vitro* over a period of years, epitomize and prove finally the main conclusions of this article, which are based on decades of research. Such metabolic analyses provide promise of a powerful tool for diagnosis of malignancy in the ever-increasing variety of tissue-culture lines now becoming available in this rapidly expanding biological and medical field, where characterization of malignancy by conventional methods (animal inoculation or otherwise) may be difficult or impracticable. This metabolic tool should be especially important in connection with the use of tissue cultures for the evaluation of chemotherapeutic agents or other control procedures.

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A university has its responsibility to the student as well as an obligation to add to knowledge. Let us not put our students in the position of observing or being a party to practices contrary to the ideal for a university and for his future career. If the student sees his institution engaged in fundamental research, freely supported and freely conducted, he will learn that independence in investigation is man's right and a university's responsibility to exemplify.—N. Paul Hudson, *Ohio State University Graduate School Record*, December 1951.

Molecular Engineering

A. von Hippel

Engineering, as taught and practiced today, applies the macroscopic and statistical laws of science. Its successes are impressive, as our technical civilization testifies; but, despite displayed vigor, the leadership is slipping from the hands of the engineer, because the power of this approach becomes exhausted.

Engineering is based on the proper use of materials. At present, with rare exceptions, such materials are selected and applied by empirical methods. With concepts of the molecular properties of matter in their infancy, this procedure was the only feasible one. However, about 50 years have now passed since the inception of the quantum theory; physics and chemistry have arrived at quantitative statements about the structure of atoms and molecules and their interaction in gases, liquids, and solids. And yet, visits to engineering laboratories and discussions with contracting agencies of the Government make it obvious that very little of this knowledge is alive in the mind of most engineers. The answers to the increasingly excessive demands for materials remain empirical; they are slow in coming and are bought in uncertain approaches at an excessive cost. It is time to introduce a more fundamental foundation on which a more powerful technology can be erected.

The transition from the phenomenological approach to matter to a "molecular engineering" has to be pioneered by the universities in a new teaching and research program that forgets about boundaries between departments as well as those between schools of science and engineering. It requires the generous cooperation of industry; it requires retraining of engineers in summer courses and by postgraduate fellowships; and last, not least, it requires a modest appraisal of the present capabilities of the new methods in competition with the established ones. In cases of great complexity, empirical experimentation may frequently still reach its goal faster than scientific analysis and synthesis. But the balance of power will shift rapidly to the molecular engineer as knowledge and experience grow.

Many others in the fields of science and engineering are obviously aware of this situation, as, for example, last year's conferences at the University of Illinois and Carnegie Institute of Technology testify. The ideas expressed in this article, which are based on our experiment at Massachusetts Institute of Technology, are intended to be a modest contribution to a general discussion.

What is molecular engineering? It is a new mode of thinking about engineering problems. Instead of taking prefabricated materials and trying to devise engineering applications consistent with their macroscopic properties, one builds materials from their atoms and molecules for the purpose at hand. This approach gives the engineer a true spiritual connection with modern science, a partnership, and a new freedom of action. He can conceive devices based on ideal characteristics and then, returning to the laboratory, inquire how far such characteristics can be made to order. He can play chess with elementary particles according to prescribed rules until new engineering solutions become apparent. He can be selective by insight, foreseeing inherent limitations of materials and making use of their actual capabilities.

This solving of puzzles on the molecular scale requires the mind to develop a kind of spiritual x-ray machine that perceives behind the macroscopic boundaries of matter its elementary constituents in action. To clarify the procedure, let us assume a technical challenge and outline the response that engineering might make both in the traditional manner and according to the new mode of thinking.

Approaches to a Technical Challenge

Airplanes of the future will travel much faster and higher through the atmosphere than today; in consequence, they will heat up by friction to a very uncomfortable temperature, say 1000°F. Can the metals used in air vehicles now, the fuel serving for their propulsion, and the electric machinery developed for their control operate safely at such elevated temperatures? Obviously not. Hence a major industrial effort is required, comprising all aspects of engineering, to translate such a plane into reality.

A standard approach would be to gather the available macroscopic information on metals as to tensile strength, on fuels concerning explosion temperatures, on insulators as to electric failure, on polymers concerning plasticity and decomposition temperatures, and so forth. By analyzing such data, one would probably find that no performance characteristics have been measured at these high temperatures and under the vibration conditions of modern jet planes, that no obtainable material will qualify, but that some trends toward improved materials are discernible. In consequence, test programs evaluating high-temperature performance are initiated under Government contracts in various industries; one modification after the other is tried and found wanting; but slowly, by bulldozer tactics, the view is cleared and the goal comes in sight.

Now, if we are lost in the woods, we need not level the forest to gain a clear view, we can climb trees and take our bearings. This the molecular engineer would do. He knows of atoms and how they are bound together, from the small diatomic molecules of gases to the ring and chain molecules of chemistry and to the glasses and crystal structures of solid-state physics. He can inform himself about the strength of the bonds that hold these particles in place and thus can evaluate which types of materials might have any chance to qualify at the anticipated high-temperature level. Next, the stability of such materials in the chemical environment found at high altitudes has to be considered; the choice is narrowed step by step, as, in addition, mechanical and electric performance requirements are introduced. Thus, by thinking about the molecular structures of materials and by a few decisive experiments to provide missing data, the possible building stones can be selected from which the required materials might be made.

After this prestudy has been made, a molecular analysis is required of the macroscopic phenomena to be controlled for safe operation of the aircraft: tensile strength, explosion temperature, electric failure, plasticity, and whatever else enters. What from a macroscopic point of view appears as a simple event, measured by a simple test and described by some simple parameters, is actually the outcome of complicated molecular events

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that, depending on circumstances, may take a variety of courses. Here lies the main fallacy of macroscopic testing: the belief that a material of the same chemical composition or trade name, subjected to the same test conditions, should give the same result. It frequently does not! For example, the mechanical or electric strength of materials thus measured varies within such wide limits that only a statistical evaluation can hide the bankruptcy of this test approach.

A scatter of test data beyond the errors of our equipment is a sure indication that the phenomena under investigation contain unrecognized and, therefore, uncontrolled parameters. These parameters are generally of a molecular nature and, hence, are invisible to the classical engineer like the ghosts in Topper's television show. Let us conjure some of them for public scrutiny.

Impurities

In composing metals, plastics, glasses, and crystals, billions upon billions of identical building stones must be set by natural processes into prescribed patterns. Obviously, this requires that only these stones are at hand, but what chemist could prepare his starting materials with that purity? "Chemically pure" reagents usually contain parts per thousand of foreign matter; the starting materials of industry embody several percent of unwanted constituents; and these extraneous particles somehow have to be accommodated.

How they will be incorporated depends on the method of preparation. For example, if a rock salt crystal grows slowly over thousands of years, as it does under natural conditions, the atoms of sodium and chlorine, because they fit the lattice structure best, are selectively inserted. The foreign matter is pushed along by street-cleaner techniques and now and then discarded in pockets. This method of purification by fractional crystallization, here carried by natural processes to the extreme, produces a rock salt crystal of great apparent purity, as optical absorption measurements testify. But take the same crystal, heat it to a few hundred degrees and cool it again, and its transparency in the ultraviolet has been greatly impaired. The discard has seeped out of its pockets and the material is now inferior to any crystal grown with reasonable care in a few hours in the laboratory. This is also borne out by conductivity measurements: before heating, the crystal is a very good insulator; after heating, its conductivity increases by orders of magnitude.

Since we are bound to operate with impure materials, it depends on preparation and requirements how disturbing this fact proves to be. In table salt, impurities in the order of several percent may not matter, but even here, who actually knows? Ailments such as cancer might be induced by impurities in our food or in the air we breathe, just as a crystal can be poisoned by the atmosphere in which it grows. Through impurities and their mode of distribution, the prehistory of a material enters as an important variable in critical performance tests.

Dislocations

The influence of prehistory is not limited to the distribution of extraneous matter only. Even ideal purity could not create or maintain an ideal material. When building stones are set endlessly on building stones, mistakes are bound to occur. Suddenly, here is an extra row of atoms that has to end in a blind edge; there is a hole in the structure we forgot to fill; and over there a row of atoms must be pivoted around a corner. These mistakes, called dislocations, will become more numerous the faster nature works —that is, the higher the temperature. As the result of statistical laws, atoms will be missing from their regular lattice sites with a probability increasing exponentially with temperature, and they will be misplaced to surfaces or interstitial positions.

In consequence, a material at any temperature level can be characterized by an equilibrium of disorder; but it takes time to create a predictable amount of confusion. As the temperature is lowered, this time lengthens exponentially from seconds to minutes, days, years, and centuries. Only by creating a material at low temperature can we therefore hope to produce the improved order realizable at that temperature level. This is the secret of why "cold rubber" tires are superior to those made by the hot vulcanization process. In general, materials will contain a disorder that is "frozen in" from some higher temperature.

Use of Imperfections

If imperfections have to be taken in stride, why not use them to advantage? After all, we pay more for a hand-woven Persian carpet than for a machine-made one, because the irregularities of the former reflect the artistic sense of its maker and replace endless repetition by ingenious variation. A perfect crystal would prove similarly uninteresting. Nonmetals would not conduct or fluoresce, ferromagnetics would not show a useful magnetic response, steel could not be hardened, even trees might not grow or life originate in such flawless surroundings. To be sure, perfection has some striking advantages—the mechanical strength of metals, the electric strength of insulators, and the moral strength of human beings could be raised a hundredfold—but adventures in life and nature arise from imperfections.

Many deviations from perfection occur besides impurities and misplaced lattice points. Electrons and electron defects, for example, may enter a dielectric from the electrodes or be generated in the volume by dissociation. These electric charges, moving combined with mass particles as ions or striking out on their own with all kinds of velocities and laws of motion, are the active ingredients of our modern electronic devices and will lead to a host of others yet to be invented. They also are the key to such chemical puzzles as: why certain compounds cannot be made in stoichiometric proportions; how colors fade and photographic films operate; how certain catalysts work; and why many tricks of the organic chemist prove to be successful.

Boundaries are imperfections, providing the highways for surface conduction, diffusion, and chemical attack. Filled with intercrystalline cements, they may be the focus of embrittlement by mechanical vibration and chemical transformation; metal fatigue and catastrophic failure result. Boundaries cause heat insulation: a single crystal of quartz conducts heat like iron by passing it on through its lattice vibrations. Disorder destroys the periodicity of motion and scatters these vibrations; hence, fragmentation and glass formation lead to the silicate materials that insulate our houses. Special boundaries, the domain walls, impart usefulness to ferroelectrics and ferromagnetics. Motion of these walls caused by external fields gives us control over the stored electric and magnetic energy and leads to the memory devices on which the success of modern computing machines depends.

There is no end to the variability of the real structure of matter and to the possibilities offered by its control. We have not even mentioned how the elementary building stones themselves, the 90-odd different atoms, can enter the design patterns of materials in endless substitutions, from the homeopathic doses of parts per billion that are required for transistors to the large-scale replacements as in mixed crystals, glasses, and metal alloys. But let us return to our airplane problem and draw some conclusions from this glance into the molecular world.

Conclusions

Our faith in the beliefs and test procedures of the classical engineer has been shattered. The test data published in the

literature are not binding as soon as they concern structure-sensitive properties. A material is not characterized by its chemical composition alone; its prehistory and the detailed arrangement of its building stones enter decisively. Taking apart a material by chemical analysis destroys the clues as effectively as the police would if they cleaned up a murder house with soap and water. Engineers have to become detectives who are familiar with sensitive nondestructive tools, including x-ray analysis, spectroscopy, electric and magnetic measurements of all kinds, and the new probing methods of nuclear-, para-, and ferromagnetic resonance.

Phenomena such as mechanical strength and metal fatigue, explosion hazard and electric failure, decomposition of plastics and loss of ferromagnetism, which are decisive for design considerations of the airplane of the future, are structure sensitive; only molecular analysis will bring them under control. Much of the needed information has been acquired by the scientists; much more is still missing. However, the incompleteness of the art does not give an excuse to let the engineer spend a further generation in the bleachers before he enters the arena. His game is being played now by stand-ins, the physicists and chemists. Only by enlisting him as an active partner in molecular thinking can we prevent squandering of our resources in antiquated approaches.

According to our experience, this educational problem is not solved by a few more courses in the science departments. If the physicist, for example—and I am one of them—talks to an engineering student in typical lingo and aloofness, the information generally passes straight through the skull, ear-in ear-out, without leaving any permanent impression. What we try to create as our answer to this situation are truly interdepartmental laboratories for molecular science and engineering. The strong foundation is fundamental research leading into the unknown for the sake of knowledge only. After new knowledge has been acquired, questions can legitimately be asked about its practical implications. Thus, from the first floor of the house, mainly populated by scientists, we reach the second, where one dreams of long-range applications. Finally, when the implementation stage has been reached, the problem passes to the top floor for the development of prototypes.

Such a laboratory structure challenges any kind of talent found in schools of science and engineering, from mathematician and theoretical physicist to the wizard of devices. Here the physicist cannot explain away difficulties with impunity, the engineer's prototype does not work, and a real answer is required. Here the ceramicist cannot persist in his old-established methods of handling materials. The scientist, inquiring into phenomena of a new order of complexity, sees what single crystals can accomplish and asks why ceramics cannot compete. Here is a feedback between all activities, stimulating thinking and critical appraisal. The modern research tools of science and engineering, when combined in one laboratory, allow a more searching approach from many angles, and the specialists able to handle them work as allies. There is no excuse for doctoral students to remain narrow minded; their research problem fits into a broad context and may be pursued with any promising tool of any discipline under expert guidance.

This effort can succeed only if the over-all problems attacked are broad and challenging and if the staff members have full freedom in their individual research and receive full credit for their contributions. The Laboratory for Insulation Research at Massachusetts Institute of Technology has been built up since 1937 as a pioneering test case. Its present staff consists of physicists, chemists, electrical engineers, and ceramicists; we hope to form an alliance with mechanical and chemical engineers, metallurgists, and biologists as experience and confidence grow. The name of the laboratory is somewhat misleading; it was originally chosen to emphasize a connection with the problems of the electrical engineer. However, there exists no true "insulation" either in electric equipment or in human affairs. Any material can be made to conduct electricity; and the generation, motion, and control of charge carriers in gases, liquids, and solids, with all transitions from insulators to metals, is one of our broad fields of interest. Other long-range projects concern the origin and action of electric and magnetic moments, from individual electron clouds and nuclei to the cases of extreme coupling, the ferroelectrics, and ferromagnetics. In short, we try to contribute to the fundamental understanding of the electric and magnetic properties of matter and to their circumspect application in engineering devices.

If laboratories for molecular science and engineering are established on a broader scale and their aims are supported by teaching on an interdepartmental level, does this solve the problem that Government and industry face in learning and applying with dispatch the concepts of molecular engineering? Obviously, the students thus educated will make their impact but only gradually. Summer-session courses and postgraduate fellowships have to be added to bring promising men back from industry to the universities for days or a year of unhampered study as coworkers in these challenging laboratories. Returning to their organizations, they will spread the new comradeship and understanding cooperation between science and engineering in molecular thinking. As a step in this direction, a 10-day course in molecular engineering will be offered at Massachusetts Institute of Technology in the summer session of 1956.

The experiments adduced by Dr. Franklin in support of his hypothesis were most ingeniously contrived and happily executed. A singular felicity of induction guided all his researches, and by very small means he established very grand truths. The style and manner of his publication are almost as worthy of admiration as the doctrines it contains. He has endeavoured to remove all mystery and obscurity from the subject; he has written equally for the uninitiated and for the philosopher; and he has rendered his details amusing as well as perspicuous—elegant as well as simple.—SIR HUMPHRY DAVY. Quoted by E. N. da C. Andrade, in "The scientific work of Benjamin Franklin," *Nature* 177, 61 (1956).

News of Science

AAAS Headquarters

The new AAAS headquarters will be ready for occupancy late this spring. The association will use the first two floors of the building, and the third floor will be shared by several affiliated societies.

The architects, Faulkner, Kingsbury and Stenhouse, have designed the building with unusual attention to thermal controls. Three sides of the structure have two-story aluminum louvers covering the windows. These provide good natural light and at the same time reduce the cost of air conditioning by deflecting the sun's rays.

The louvers are operated by an electric motor and a clock mechanism; the angle of the aluminum panels changes with the movement of the sun. The timing device will probably have to be adjusted about six times a year so that the windows will always be shaded. The louvers have created considerable interest, for, although they have been used on the West Coast, this is the first time that they have been tried in the Washington area.

All mechanical equipment for the new structure is enclosed in the penthouse—for example, the air conditioning and heating units and the elevator shaft.

The two photographs, showing the back corner of the building at 15th and N Streets and the front corner at 15th Street and Massachusetts Avenue, were taken by Kenneth Gilmore of the *Washington Daily News*.

Radiation in Emission Nebula

The first observation of the absorption of 3.5-meter radiation in an optical emission nebula, NGC6357, was reported in the 28 Jan. issue of *Nature* by B. Y. Mills, A. G. Little, and K. V. Saeritan of the Australian Commonwealth Scientific and Industrial Research Organization. This absorption of radio waves in an emission nebula leads to an estimate of the electron temperature of the nebula that is based almost entirely on radio data.

The authors have come to the conclusion that the electron temperature in the nebula is 6500°K. This is somewhat lower than the 10,000°K that is usually assumed for such nebulae. The value could be even lower if the nebulae are "patchy." A quantitative optical study is suggested.

$2,657,434 for Medical Schools

Grants amounting to $2,657,434 were awarded to the nation's 81 medical schools for 1955 by the National Fund for Medical Education. Fifty-eight percent was contributed by corporations, through the fund's Committee of American Industry, and the balance by physicians, through the American Medical Education Foundation.

This is the largest annual award in the fund's history, 22 percent greater than in 1954, and brings to $9,589,490 the total collected by the fund since 1951, the year in which the first grants were awarded.

Each of the 75 4-year schools received $15,000 and $30 for every undergraduate medical student; each of the 6-year schools received $7500 and $30 per student. Added to these grants were the gifts of individual physicians to designated schools.

Fund grants are unrestricted, except for the provision that they cannot be used for building purposes. The money is used by the schools primarily to increase teacher salaries, fill faculty vacancies, and open new courses in areas of recent scientific progress.

Industry's support of medical education has mounted steadily since 1949, when the fund was established. Last year 1532 corporations contributed to the fund, compared with 1129 in 1954.

Size of the Antiproton

The antiproton, newly discovered particle of negative matter [*Science* **122**, 1222 (23 Dec. 1955)], is twice the size scientists expected, according to Owen Chamberlain of the University of California in a report that he delivered at the recent meeting in New York of the American Physical Society. In connection with this finding, Edward Teller, also of the University of California, has predicted the future discovery of two new particles. He says that the undiscovered particles are needed to explain the large effective size of the antiproton.

Chamberlain reported that more examples of the antiproton are now being found, for investigators are learning exactly where to place the emulsions on which the negative particles register as nuclear stars. One star, discovered by Gerson Goldhaber and associates, is especially important. It has eight prongs, with three protons and five pions. One pion decays into a mu meson and an electron. Total visible energy of this star is 1230 Mev, an amount that is in excess of the rest mass of either the proton or antiproton, which is 938 Mev.

This excess energy gives the best evidence yet that the antiproton annihilates either a neutron or a proton. This is demonstrated by the fact that the visible energy exceeds that of one particle. The difference between 1230 Mev and the 1876 Mev of two particles is the energy of neutral particles not visible that emerge from the star.

The Berkeley group is collaborating with Eduardo Amaldi and his coworkers in Rome. The antiproton star reported by Amaldi's group showed a visible energy of 826 mev.

News Briefs

■ A report on venereal disease that was released jointly by the Association of State and Territorial Health Officers, the American Venereal Disease Association,

and the American Social Hygiene Association shows that in 1955 25 states and 14 major cities had increases in the attack rate of syphilis or gonorrhea, or both. The record was published in an effort to persuade the Congress to appropriate a minimum of $5 million to combat venereal disease in 1957. The current budget requests $3.5 million, which is the same as the amount authorized for 1956.

■ The Franklin Institute Laboratories for Research and Development are constructing an especially long infrared cell and spectrometer to be used for studies of air pollution and smog in the Los Angeles area. The infrared equipment will be housed in a special mobile laboratory. It is hoped that construction work will be completed by September, when Edgar R. Stephens, group leader for air pollution research at the institute, plans to direct field studies.

■ Gerard P. Kuiper of Yerkes Observatory, Williams Bay, Wis., reported recently that the solar system has eight planets, not nine. Kuiper says that Pluto, regarded as the ninth planet, "in reality is only one of Neptune's satellites or moons, which broke away untold millions of years ago." He bases his conclusion on his own findings and on those of Merle Walker and Robert Hardie of the Lowell Observatory at Flagstaff, Ariz. Pluto differs from genuine planets in its small size, its eccentric orbit, and its comparatively slow rotation.

■ A technique for soldering aluminum, stainless steel, glass, and ceramics without special equipment has been developed at the Los Alamos Scientific Laboratory. The new method of joining these materials is expected to be much more economical than the ultrasonic method that is now in use.

■ For the general use of science, industry, and administration, a computation center is to be opened this spring in Frankfurt, Germany. A Remington Rand UNIVAC, the first in Europe, will be installed in the Battelle Institute.

■ Acheson Industries, Inc., New York, has announced that 9 Mar. is the 100th anniversary of the birth of Edward G. Acheson, known internationally for his discovery of methods for producing silicon carbide, synthetic graphite, and colloidal graphite, which revolutionized industry. Acheson, who died in 1931, was a fellow of the AAAS.

Another centennial celebration is that of the discovery of the first synthetic dye. In 1856 William Henry Perkin produced crystals of mauve, a development that proved to be the foundation upon which the existing aniline dye industry was built. Lead by the American Association of Textile Chemists and Colorists and supported by 27 chemical, technical, and scientific societies, the centennial will be observed by chemists throughout 1956.

■ Creation of the American Sanitary Engineering Intersociety Board has been announced by representatives of several major national engineering and public health organizations. They constitute a Joint Committee for the Advancement of Sanitary Engineering, under the chairmanship of Earnest Boyce, head of the University of Michigan Department of Civil Engineering.

The new body has been organized and incorporated "to improve the practice, elevate the standards and advance the cause of sanitary engineering; to grant and issue to engineers, duly licensed by law to practice engineering, certificates of special knowledge in sanitary engineering or in any field thereof." Headquarters have been opened in the Engineering Societies Building, 33 W. 39 St., New York.

Scientists in the News

The annual report of the Borden Company Foundation, Inc., lists the recipients of the $1000 research awards for 1955 and the organizations that administer them: American Dairy Science Association, CLIFFORD W. DUNCAN, Michigan State University, for contributions in the area of biochemistry and nutrition in dairy animals, and FRANK V. KOSIKOWSKI, Cornell University, for studies in the area of cheddar cheese ripening; American Chemical Society, FRED HILLIG, Food and Drug Administration, for his role in the development of chemical methods of analysis for dairy products; American Institute of Nutrition, ALBERT G. HOGAN, University of Missouri, for research on vitamin requirements and the discovery of vitamin B_c; American Academy of Pediatrics, L. EMMETT HOLT, JR., New York University College of Medicine, for contributions to infant nutrition; Association of American Medical Colleges, CHARLES HUGGINS, University of Chicago, for research on the relationship between the endocrine glands and cancer; American Veterinary Medical Association, HARRY E. KINGMAN, Wyoming Hereford Ranch Foundation (retired), for contributions to the knowledge of fertility and disease in cattle; Poultry Science Association, MARLOW W. OLSEN, U.S. Department of Agriculture, for studies of hatchability and fertility in poultry; American Home Economics Association, PEARL P. SWANSON, Iowa State College, for fundamental studies of the basic problems of human nutrition.

SYLVAIN J. PIRSON, who since 1949 has been a special research associate for the Stanolind Oil and Gas Company, Tulsa, Okla., and a special lecturer in petroleum engineering at the University of Tulsa, has joined the faculty of the University of Texas petroleum engineering department.

GEOFFREY W. RAKE, medical research consultant to the E. R. Squibb and Sons Division of the Olin Mathieson Chemical Corporation and research professor of microbiology at the University of Pennsylvania School of Medicine and Veterinary Medicine, has been appointed scientific director of the International Division of Olin Mathieson. In his new post Rake becomes responsible for all pharmaceutical, medical, and veterinary research conducted outside of the United States by the company's Squibb International Division.

The following ten physicians and surgeons have each received *Modern Medicine*'s citation for distinguished achievement in medicine: I. S. RAVDIN and PAUL GYORGY of the University of Pennsylvania; STANLEY COBB and JOHN F. ENDERS of Harvard University; WARREN H. COLE of the University of Illinois; FRANK H. KRUSEN of the Mayo Clinic; IRVINE H. PAGE of the Cleveland Clinic; JONAS E. SALK of the University of Pittsburgh; GEORGE H. WHIPPLE of the University of Rochester; and IRVING S. WRIGHT of Cornell University.

JOHN C. GRIFFITHS, professor of petrography in the College of Mineral Industries at Pennsylvania State University, has succeeded P. D. KRYNINE as head of the department of mineralogy.

NORMAN W. KARR, for the past 3 years director of clinical research at Riker Laboratories, Los Angeles, Calif., has joined the Squibb Institute for Medical Research, New Brunswick, N.J., as an assistant to the director of the research and development laboratories.

BYRON T. SHAW, administrator, Agricultural Research Service, U.S. Department of Agriculture, has been designated United States member of the Technical Advisory Council of the Inter-American Institute of Agricultural Sciences. CLAUD L. HORN, agricultural attaché, American Embassy, San José, Costa Rica, has been named alternate U.S. member of the council.

The purpose of the Inter-American Institute of Agricultural Sciences is "to encourage and advance the development of agricultural sciences in the American Republics through research, teaching and extension activities in the theory and practice of agriculture and related arts

and sciences." The institute carries on its program through (i) demonstration of modern agricultural techniques, (ii) research and field projects carried on by resident and visiting scientists, (iii) instruction at the graduate level of students who are selected with a view to their returning to their own countries to occupy scientific and administrative positions, and (iv) inter-American technical meetings.

OWEN H. WAGENSTEEN, professor of surgery at the University of Minnesota, will deliver the ninth annual Rudolph Matas lecture at Tulane University on 12 Mar. The lecture is presented each year by the Beta Iota chapter of Nu Sigma Nu.

PAUL WEISS of the Rockefeller Institute for Medical Research delivered the 20th annual Adam M. Miller memorial lecture at the State University of New York College of Medicine on 2 Feb. He discussed "Prospecting in the field of growth and differentiation."

HERBERT J. STACK, director of the Center for Safety Education at New York University, delivered the 31st Hermann M. Biggs memorial lecture of the New York Academy of Medicine on 2 Feb. He discussed the "Psychology of drivers."

BERNARD DAVIDOW, former chief of the acute toxicity branch in the Division of Pharmacology of the U.S. Food and Drug Administration, has been appointed director of pharmacology for the newly established laboratories of the New Drug Institute, 130 E. 59 St., New York. The institute serves industry in all phases of drug research and development. Davidow will direct pharmacological and toxicity investigations on new drugs, food additives, and cosmetic ingredients.

The following are among those who have recently received honorary doctoral degrees.

Wayne University: JACK A. MORTON, director of Device Development, Bell Telephone Laboratories.

University of Pennsylvania: HUGO THEORELL, head of the Biochemistry Department of the Nobel Institute in Stockholm.

Birmingham Southern College: ERNEST V. JONES, consultant to Oak Ridge National Laboratory.

ELMER W. ENGSTROM, senior executive vice president of the Radio Corporation of America who is in charge of the concern's research laboratories at Princeton, N.J., received the 1956 John Ericsson gold medal on 11 Feb. at the 68th annual dinner of the American Society of Swedish Engineers in New York. The medal is awarded every other year to a Swedish citizen, or to an American citizen of Swedish descent, in recognition of technological or scientific contributions.

LORIN E. HARRIS, professor of animal husbandry and chairman of the Institute of Nutrition at Utah State Agricultural College, left this month for Australia, where he will conduct research on sheep nutrition under a Fulbright fellowship.

Another Utah Fulbright scholar is DATUS M. HAMMOND, chairman of the department of zoology, entomology, and physiology, who is at present in Germany at the University of Munich studying trichomoniasis in cattle. He is scheduled to return to the United States early next fall.

LESTER E. KLIMM, professor of geography at the University of Pennsylvania, received the Henry Grier Bryant gold medal of the Geographical Society of Philadelphia at the society's annual dinner on 14 Feb. The medal is given for distinguished service to geography.

HAROLD CHATLAND, now dean of the College of Arts and Sciences and professor of mathematics at Montana State University, became acting dean of the faculty on 1 Feb. A. S. MERRILL, who has been both dean of the faculty and vice president, will continue as vice president.

F. W. BLAIR, director of research and development for the Procter and Gamble Company, retired on 1 Jan. after 38 years of service. Blair received his undergraduate training in chemistry at Amherst College and his graduate training at Princeton University.

He began his career with Procter and Gamble at the Ivorydale factory in Cincinnati in 1917, and 3 years later went to Kansas City as plant superintendent. In 1921, he returned to Cincinnati to take charge of the work of standardizing factory operations and laboratory control; later he directed process development, and started and directed the products service department in the newly created chemical division.

He was made chemical director in 1928 and served in that capacity until 1953, when the chemical division was absorbed into the new research and development department, at which time he became director of research and development. Under Blair's direction Procter and Gamble's research and development program has grown from a comparatively small operation into a major division of the company.

Recent Deaths

HENRY BEEUWKES, St. Petersburg, Fla.; 74; director of the West Africa Yellow Fever Commission, 1924–34; formerly conducted research on tuberculosis at Cornell University Medical College; World War II organizer and commander of the Valley Forge General Hospital; 31 Jan.

EMILE BOREL, Paris, France; 85; professor of mathematics at the University of Paris 1909–41; vice-president of the International Council of Scientific Unions, 1946; 4 Feb.

HENRI CHRETIEN, Washington, D.C.; 77; optical engineer; codesigner of the telescope for the United States Naval Observatory in Washington, D.C.; inventor of the anamorphic lens used as a basis for the CinemaScope film process; 6 Feb.

WALTER C. COFFEY, St. Paul, Minn.; 80; authority on animal husbandry; president emeritus of the University of Minnesota; vice president AAAS Section O in 1930; 31 Jan.

REUBEN FRIEDMAN; Philadelphia; 63; internationally known dermatologist and author; professor of clinical dermatology at Temple University Hospital; 4 Feb.

FRANK C. HOCKEMA, Lafayette, Ind.; 63; mechanical engineer; vice president of Purdue University; 3 Feb.

DAVID LAZARUS, St. Petersburg, Fla.; 72; former professor of obstetrics and gynecology at New York Polyclinic Medical School; 6 Feb.

MALCOLM T. MacEACHERN, Chicago, Ill.; 74; associate professor of medicine at Northwestern University, Medical School, 1943–48, and founder of the program in hospital administration at the school; 3 Feb.

ERICH A. MARX, Troy, N.Y.; 81; professor of physics at Rensselaer Polytechnic Institute; former professor of science at the University of Leipzig; 31 Jan.

GEORGE OENSLAGER, Akron, Ohio; 82; research authority on rubber chemistry; 5 Feb.

LLOYD M. SALISBURY, Montville, N.J.; 66; civil engineer; 1 Feb.

GROVER C. SAYER, Hillside, N.J.; 69; former engineer for Esso Research and Engineering Company; 5 Feb.

Education

■ The University of Rochester is establishing a computing center. Its facilities will include one of the new Burroughs E 101 machines, which is to be installed soon, and an IBM 650 electronic computer, to be received next summer. The university is organizing a new computing group and training program. The project

was authorized after a 5-year study of computer equipment and techniques by representatives of the university and of local companies in the optical, banking, retail, machine tool, and electronic fields.

■ Gifts totaling $1 million have recently been received by Washington University (St. Louis) to endow a neurology institute in the School of Medicine. Half of the money was from the Louis D. Beaumont Foundation of Cleveland, Ohio. The rest was contributed by Morton J. May, chairman of the board of the May Department Stores Company, and by Mrs. Charles M. Rice, who made the gift in memory of her late husband. The new unit, the Beaumont-May Institute of Neurology, will be devoted to study of chronic brain disorders.

■ A $100,000 ornithology center is to be built next spring in Cornell University's Sapsucker Woods, 3 miles from the campus center. An observation room, with picture windows overlooking a pond, woods, and feeding stations, will connect with a new ranch-type building containing offices, laboratories, and workrooms.

Although ornithology students have used Sapsucker Woods for many years, the university acquired it only last year through gifts by the families of Lyman K. Stuart of Newark, N.Y., and Walter Heasley of Ithaca.

The Laboratory of Ornithology, for 40 years a unit under the entomology, zoology, and conservation departments, successively, is now an independent department of the university. It will continue to direct ornithological expeditions throughout the world. This year the Cornell Trust for Ornithology is sponsoring Mr. and Mrs. Donald McChesney of Syracuse, N.Y., and Mr. and Mrs. James Pass of Cazenovia, N.Y., on an expedition to Kenya, where they will make films and recordings of East African birds.

■ Texas business and industry is helping the University of Texas to organize a summer course for junior and senior high-school teachers. The program is to be offered in the first term of the 1956 summer session. Professors in the natural sciences and mathematics and specialists in teaching methods will join with special lecturers from business and industry for the program. Many companies will provide scholarships for local teachers, and others will make available exhibits and special materials. Visits to industrial plants and research installations will supplement classroom sessions.

Two types of teacher are intended to be served by the program: experienced science and mathematics instructors who wish to be brought up-to-date on developments in their fields, and teachers with limited formal training who would like to take courses to prepare them for more effective teaching. Robbin Anderson, of the university's department of chemistry and chairman of the Committee on Science Teaching which evolved the plan, has announced that a wide variety of courses and seminars will be offered.

■ The Biology Council of the National Academy of Sciences–National Research Council has prepared a booklet entitled *Career Opportunities in Biology*. Row, Peterson and Company, publisher in this nonprofit enterprise, will send a copy of the booklet to every junior high school, high school, and college in the country during March.

Russell B. Stevens, executive secretary of the Biology Council, is author of the new booklet. He estimates that for every full-time research biologist, teacher, civil servant, or administrator, there is a need for three to five persons as technicians, clerical workers, laboratory aides, student assistants, animal caretakers, and so forth. There is also a place in biology for mathematicians, agriculturists, businessmen, artists, writers, librarians, and persons with mechanical aptitudes and skills. The foreword for the publication is by Paul A. Weiss, head of the Laboratory of Developmental Biology at the Rockefeller Institute for Medical Research, under whose chairmanship the booklet was prepared.

■ The French National School for Geographic Sciences (Ecole Nationale des Sciences Géographiques) will again offer a theoretical and technical course in aerial photogrammetry. This program is particularly suited to non-French students and photogrammetrists who desire to familiarize themselves with the instruments and methods currently used in France. The course will be held at Saint-Mande (near Paris) from 4 June to 13 July, making it possible for participants to attend the eighth International Congress for Photogrammetry in Stockholm. Although lectures will be delivered in French, explanations will be provided in English and in Spanish.

The number of participants is limited to 25. Applications for registration must be sent *before 15 May* to Monsieur le Directeur, l'Ecole Nationale des Sciences Géographiques, 2, Avenue Pasteur, Saint-Mande (Seine), France.

■ An electron microscope has been presented by the Japanese Government to the University of California at Los Angeles. The microscope, which was made by Hitachi, Ltd., of Tokyo, was given to the department of infectious diseases to foster friendly relations between American and Japanese scientists, and to honor Japanese scientists who have been associated with the department. The instrument is being installed in a special laboratory made possible primarily through gifts from the Nina Anderton Foundation and Myron Prinzmetal.

■ The School of Agriculture of the William H. Miner Agricultural Research Institute at Chazy, New York, is scheduled to open on 4 Sept. A 1-year course in general agriculture will be offered to students of the area.

Enrollment is limited and candidates will be accepted on the basis of interest and adaptability. There is no tuition fee. Books, meals, and dormitory housing will be furnished without charge.

Practical agriculture will be stressed. It is the aim of the institute to train students so that, through application of their learning, the productivity of the land will be increased, the work can be done with less labor, and the economic status of the farmers of the area will be improved.

Staff positions for vocational agricultural teachers or specialists are available. Address communications to Edward J. Czarnetzky, Dean of Agricultural Education, School of Agriculture, Chazy, N.Y.

■ Forty high-school seniors have been named finalists in the 15th annual Science Talent Search. Winners were selected from a group of 20,828 aspirants, highest number in the history of the scholarship competition. The eight girls and 32 boys are being awarded all-expense trips to Washington, D.C. They will arrive in Washington on 1 Mar. to take part in the 5-day Science Talent Institute, during which top winners will be selected and the Westinghouse science scholarships awarded.

This year New York continued to lead all states in the number of winners produced—five boys and two girls. Five of the seven come from New York City and vicinity. California won second place with four finalists, all boys, one of whom attends school in Exeter, N.H. Illinois, Indiana, and Minnesota tied for third place with three winners each. Four states will send two winners each, and eleven are represented by one winner each.

Begun in 1942, the Science Talent Search is conducted by Science Clubs of America through Science Service. Awards are made by the Westinghouse Educational Foundation, which is supported by the Westinghouse Electric Corporation.

■ The Cold Spring Harbor Biological Laboratory will offer three specialized courses during the summer of 1956: bacterial viruses, 18 June–7 July; genetics of fungi, 11–31 July; and bacterial ge-

netics, 2–22 Aug. The course on genetics of fungi is being offered for the first time this year, and G. Pontecorvo of the University of Glasgow will be in charge.

A limited number of fellowships covering part of the tuition fees will be available for graduate students. In addition, research facilities for work on microbial genetics throughout the summer will be available to a limited number of independent research workers. Information may be obtained from the Biological Laboratory, Cold Spring Harbor, New York.

Grants, Fellowships, and Awards

■ Rand McNally and Company will offer 25 full-tuition scholarships to teachers and supervisors in elementary and secondary schools for a workshop in geography at the Northwestern University summer session. The scholarships are part of the Rand McNally centennial, which is being observed throughout 1956.

Offered in cooperation with Northwestern's School of Education and department of geography, the scholarship program is intended to enable teachers to explore new concepts in the field of geography. Applications must be filed *by 1 Apr.* The Geography Workshop will be held on the Evanston campus from 25 July to 3 Aug. Applications and additional information may be obtained from the Dean, School of Education, Northwestern University, Evanston, Ill.

■ The New York Botanical Garden has announced the Gertrude S. Burlingham fellowship in mycology for advanced predoctoral or postdoctoral summer study at the garden. The stipend is $700; work under this appointment may begin at any time after 1 June and should continue for approximately 3 months. Nominations or applications should reach the director *by 15 Apr.*

■ The Cancer Research and Hospital Foundation has announced its annual Sherman Pratt fellowship for clinical cancer chemotherapy. The award will be made to graduates of accredited United States or foreign medical schools who are interested in gaining experience and training in new methods of clinical cancer chemotherapy developed by the Institute of Applied Biology.

The award comprises $7000 for a 1-year fellowship, or $3500 for 6 months. Applicants should submit name, address, age, medical school, year of graduation, postgraduate experience, and background to the Sherman Pratt Fellowship Award Committee, Cancer Research and Hospital Foundation, 161 E. 90 St., New York 28.

■ The Gravity Research Foundation, New Boston, N.H., has announced the 1956 awards for essays on gravity. Five winners will be named on 1 June. They will be selected for the best 1500-word papers on the possibilities of discovering (i) some partial insulator, reflector, or absorber of gravity; (ii) some alloy, or other substance, the atoms of which can be agitated or rearranged by gravity to throw off heat; or (iii) some other reasonable method of harnessing, controlling, or neutralizing gravity. The awards will be for $1000, $300, $200, $150, and $100, respectively.

Essays, with two carbon copies, must be received *before 16 Apr.* They will be accepted from anyone who is seriously interested in the application of gravity to practical uses for the benefit of humanity. All essays must be typewritten in English on 8½ by 11-inch paper. A title covering the area of thought expressed in the essay and a summary paragraph of 100 words or less should be included, as well as a short biographical sketch.

■ National Mass Media awards for children's books were presented on 6 Feb. by the Thomas Alva Edison Foundation. *The Boy Scientist,* by John Lewellen and published by Simon and Schuster, won the Best Children's Science Book award (for younger children).

■ The James F. Lincoln Arc Welding Foundation of Cleveland, Ohio, is offering $20,000 in cash awards for ideas or suggestions that will accelerate progress in arc welding. Residents of the United States or its possessions are invited to submit ideas to the foundation on any aspect of arc welding that can be used to advance welded design, welding engineering, or the general application of the arc-welding process. No restrictions are placed on either the nature or the extent of ideas that may be submitted for award.

The $20,000 will be distributed in 20 awards with a top one of $5000; others will amount to $4000, $3000, $2000, and $1000. There will be additional smaller prizes. Ideas must be submitted *by 30 July.* Complete information and rules are available from the James F. Lincoln Arc Welding Foundation, Cleveland 17, Ohio.

In the Laboratories

■ Parke, Davis and Company has announced that it will build a new medical research center that is to cost approximately $10 million. This year will be devoted to planning; actual construction is expected to take two additional years. The exact location of the new facility has not yet been decided.

■ The American Cyanamid Company has effected the consolidation of its research activities into a single division under the direction of Kenneth H. Klipstein. Geographic regrouping has brought related activities together at the appropriate research laboratory. This consolidation is part of a divisional realignment of the company that started 2 years ago.

The research division, which has equal status with the nine operating divisions and carries out research for them, is grouping related activities in the laboratories at Bound Brook, N.J.; Pearl River, N.Y.; and Stamford, Conn.

At Bound Brook a new administration-laboratory building will house research activities primarily related to the organic chemicals and pigments divisions.

At Pearl River new construction will make it possible to centralize all research in the pharmaceutical and biological fields. The laboratories at Stamford, Conn., will carry on researches in plastics, agricultural chemicals, industrial chemicals, and mineral dressings, as well as process development and basic research in new fields.

■ The Naugatuck Chemical Division of the United States Rubber Company has acquired a 150-acre tract of land in the Scott's Bluff region of Baton Rouge, La., on which it plans to construct a new chemical plant for the manufacture of Kralastic plastic materials. Kralastic is a copolymer based on styrene, butadiene, and acrylonitrile that is used for pipe, automotive parts, and a variety of other industrial products.

■ The Southern California Edison Company will be the first utility in California to produce electricity from atomic energy. The Atomic Energy Commission has authorized Atomics International, a division of North American Aviation, Inc., and the Edison Company to negotiate a contract in connection with the Atomics International experimental reactor near Santa Susana. The company's investment in the nuclear installation will be slightly more than $1 million.

California Edison has announced that it will share the information and experience it derives from building and operating the station. To the extent permitted by the AEC, a number of representatives of both public and privately owned utilities will be allowed access to the station to obtain information on engineering features and data and to observe operating and maintenance phases of the project. Electricity from the experimental nuclear electric plant will be available for commercial use in the Santa Susana area some time during the coming summer.

■ The Spinco Division of Beckman Instruments, Inc., now located at Belmont, Calif., has broken ground in Stanford Industrial Park for a $500,000 research and development center that will be devoted to highly specialized instruments for the advancement of medicine and the diagnosis of disease. The first earth was turned by Arnold O. Beckman, president of Beckman Instruments, Inc., and the Spinco cofounders, Maurice Hanafin and Edward Pickels.

■ Plans for construction of a reactor facility at Schenectady, N.Y., have been announced by ALCO Products, Inc. To be built and equipped at a cost of about $230,000, the nuclear laboratory will be completed in May of this year. It will be located in the company's main plant. The facility will be used for nuclear experiments in connection with ALCO's contract for design and construction of the Army Package Power Reactor that is now under construction at Fort Belvoir, Va.

■ The Atomic Energy Commission has announced that the Argonne National Laboratory, Lemont, Ill., has been assigned responsibility for the design and development of a military nuclear reactor plant for production of electricity and for space heating. The commission and the laboratory have selected the Pioneer Service and Engineering Company of Chicago to work with the laboratory on the design of the reactor and the associated plant.

The project calls for the design of a low-power, heterogeneous, boiling reactor, to be known as the Argonne Low-Power Reactor (ALPR). The power plant that is proposed would produce a combined electrical and heat-energy output of several hundred kilowatts. The ALPR is planned as a prototype of nuclear plants for use in remote areas by the military services.

■ Plans for construction of a series of research laboratories on a 22-acre site at Stanford University for advanced studies in missiles and unmanned aircraft have been announced in a statement issued jointly by the university and the Lockheed Aircraft Corporation. The announcement also disclosed details of Lockheed's plan for expanding its missile systems division; this will entail a new base at Sunnyvale, Calif.

Establishment of the new missile division facilities in Palo Alto and in Sunnyvale are first steps in a research and development program in which Lockheed will invest approximately $20 million during the next 3 years. About $7 million will be spent on the first two Stanford laboratories and the initial Sunnyvale construction.

■ The research activities of Merck and Company, Inc., will be consolidated in a new division of the company, to be called the Merck, Sharp and Dohme Research Laboratories. This division will be responsible for all of the company's new product research in biology, chemistry, and medicine. Heretofore this work has been under the direction of the company's Chemical Division in Rahway, N.J., and the Sharp and Dohme Division in West Point, Pa. Max Tishler takes office on 1 Mar. as head of the new division with the title of vice president and executive director; at present he is vice president for scientific activities of the Chemical Division.

Miscellaneous

■ In the March issue of *The Scientific Monthly*, John Cockcroft writes on the "Future of atomic energy." This article is based on an evening lecture he presented at the International Conference on Peaceful Uses of Atomic Energy in Geneva last August. Other articles appearing are "History of science and the sociology of science," Herbert Dingle; "Meaninglessness of the word *protoplasm*," Garrett Hardin; "Human resources and national security," Eli Ginzberg, Edward A. Fitzpatrick, Howard A. Meyerhoff, and Eugene M. Kulischer; and reports of the AAAS Atlanta meeting. Six books are reviewed.

■ A new list of science and engineering vacancies under UNESCO's Technical Assistance Program has been released by the New York office. The following conditions apply in general to all posts: (i) salaries range from $6000 to $8400 a year, free of national income tax; (ii) lodging is furnished by the host government or a lodging allowance is provided; (iii) travel expenses of the expert are paid to duty station and back, and expenses are also paid for a wife and dependent children if a contract is for 1 year or longer; (iv) the expert, who holds the status of an international civil servant, receives annual and sick leave, hospitalization, and insurance benefits; and (v) unless otherwise specified, English is the only required language.

Current openings are for a meteorologist or geophysicist, Karachi, Pakistan; a specialist in science teaching, Taipeh, Formosa; an expert in solar energy, Heliopolis (near Cairo), Egypt; a professor of electronics, Calcutta, India; a professor of physical chemistry, Haifa, Israel; a nuclear physicist, Cairo, Egypt; two research specialists with training in sociology and social psychology, one for Rio de Janeiro, Brazil, and the other for the Philippines; a professor of sociology, Damascus, Syria; two specialists in the restoration of monuments and the conservation of archeological sites, one for Iran and the other for Pakistan; and a specialist in the use of television for adult education, France. Applications for these posts or for additional information should be addressed to the Technical Assistance Unit, UNESCO, United Nations, New York 17, N.Y.

■ Section 6 of the X-Ray Diffraction Data Card File, which is distributed by the American Society for Testing Materials, has recently been published. It is available in plain and keysort cards and covers approximately 600 new powder patterns and 600 revised and improved data patterns previously issued in Sections 1 to 5, inclusive. The Diffraction Data File is sponsored by the American Crystallographic Association, the American Society for Testing Materials, the British Institute of Physics, and the National Association of Corrosion Engineers.

A revised *Cumulative, Alphabetical and Grouped Numerical Index of X-Ray Diffraction Data* (*STP 48E*) including the new Section 6 has also been published. For information, address the American Society for Testing Materials, X-Ray Dept., 1916 Race St., Philadelphia 3, Pa.

■ The American Sociological Society, publisher of the *American Sociological Review*, has announced the publication of *Sociometry*, a journal of research in social psychology. Founded in 1937 by J. L. Moreno, this quarterly journal will become an official publication of the society with the March 1956 issue.

Leonard S. Cottrell, Jr., social psychologist, Russell Sage Foundation, will be the editor. The new *Sociometry* will report research in social psychology, and at the same time provide an outlet for the developing body of theory in this field.

The annual subscription rate is $9 for both domestic and foreign subscribers, with single issues priced at $2.25. Correspondence regarding subscriptions should be addressed to The American Sociological Society, New York University, Washington Square, New York 3. Correspondence with the editor should be sent to Dr. Leonard S. Cottrell, Jr., Russell Sage Foundation, 505 Park Ave., New York 22.

Errata: In the article "Pronuclear fusion as affected by x-rays and by postirradiation anaerobiosis," by C. S. Bachofer, in the issue of 27 Jan., page 139, the last sentence in column 1 should begin "The term ¼-fused is used to designate . . .," not "The sum ¼-fused . . ." as printed.

In the article "Magnetic techniques for *in vitro* isolation of leucocytes," by Sumner Levine, in the issue of 3 Feb., page 186, the equation should read $\mu = \sqrt{n(n+2)} = 4.90$ Bohr magnetons, instead of as printed with the square root sign covering the last part of the equation.

Reports and Letters

Lowered P/O Ratios with Mitochondria Isolated from Livers Showing Cloudy Swelling

Morphological changes in the mitochondria of cells with "cloudy swelling" (the earliest histological evidence of cellular degeneration) have been demonstrated repeatedly. A reciprocal relationship between the shape of mitochondria and the rate of oxidative phosphorylation has been shown recently (*1*). Mitochondria isolated from normal cells were used to establish this interdependence; swelling was induced either by osmotic means or by incubation under conditions in which the oxidative phosphorylation was uncoupled.

It was of interest, therefore, to study the formation of high-energy phosphate bonds in cells affected by a typical cloudy swelling such as can be produced with certain bacterial toxins. Evidence has been presented in a previous paper (*2*) that, in cloudy swelling induced by diphtheria toxin, the easily hydrolyzable phosphate is decreased. Further experiments have shown that repeated injections of 2,4-dinitrophenol, a compound well known to uncouple oxidative phosphorylation *in vitro* (*3*), produced cloudy swelling of liver and kidneys in the rat (*4*). Analogous results were obtained by injecting rats with thyroxine (*5*), which also uncouples oxidative phosphorylation (*6*). This report is concerned with the phosphorylation quotients observed with mitochondria isolated from livers that showed cloudy swelling (*7*).

Table 1. Phosphorylation quotients with mitochondria from livers showing cloudy swelling as compared with the controls. The figures represent the mean ± standard error and those in parentheses give the number of observations.

Animal	Substrate	P/O	
		Controls	Treated animals
Rat	Succinate	1.8 ± 0.07 (5)	1.3 ± 0.09 (5)
Rat	α-Ketoglutarate	3.2 ± 0.07 (10)	2.5 ± 0.16 (10)
Guinea pig	Succinate	2.0 ± 0.08 (5)	1.7 ± 0.07 (5)
Guinea pig	α-Ketoglutarate	3.1 ± 0.21 (4)	1.7 ± 0.14 (4)

In order to produce cloudy swelling of the liver, rats were injected intraperitoneally with *S. typhi murium* toxin (the smallest dose that would kill such animals in 4 days) and guinea pigs were injected subcutaneously with diphtheria toxin (1 MLD/250 g of body weight). Animals were used 24 hours after the toxin injection. In all cases, the livers were examined histologically to confirm the occurrence of cloudy swelling in the treated animals. Liver mitochondria were prepared in 0.25*M* sucrose-0.005*M* versene (ethylenediaminetetraacetic acid, adjusted to *p*H 7.4 with NaOH), essentially by the procedure of Schneider (*8*).

The results of the phosphorylation experiments are shown in Table 1. They are expressed as P/O ratios (moles of inorganic orthophosphate which disappear per atom of oxygen consumed).

The complete reaction system contained the following: mitochondria derived from 500 mg of fresh tissue; 250 μmoles of sucrose (contributed from the added mitochondria); 15 μmoles of versene (including the amount of the mitochondrial suspension); 60 μmoles of potassium phosphate buffer at *p*H 7.4; 75 μmoles of KCl; 20 μmoles of $MgSO_4$; 40 μmoles of KF; 90 μmoles of succinate or 30 μmoles of α-ketoglutarate; 3×10^{-2} μmoles of cytochrome *c*; 3 μmoles of adenosine-5′-phosphate; 78 μmoles of glucose; and 20 mg of a hexokinase preparation (*9*) in a final volume of 3 ml. A Warburg bath was used for incubation at 25°C for 20 minutes, with air as the gas phase; CO_2 was absorbed with KOH. Inorganic orthophosphate in the trichloroacetic filtrates was estimated according to Fiske and Subbarow (*10*).

It can be seen that with both succinate and α-ketoglutarate, the phosphorylation quotient was lowered when mitochondria from livers showing cloudy swelling were used. The lowering of the P/O ratios has been observed with mitochondria prepared from livers of rats treated with *S. typhi murium* toxin and also from livers of guinea pigs injected with diphtheria toxin. In the latter system, the inhibition of phosphorylation is more marked with α-ketoglutarate as a substrate than it is with succinate as a substrate.

The hydrolysis of adenosine-5′-phosphate, adenosinetriphosphate, and glucose-6-phosphate by the mitochondria was also studied; no increased rate of hydrolysis was found with the mitochondria from pathological livers. Thus, the low P/O ratios do not appear to be attributable to an increased dephosphorylation.

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2 May 1955

2-Methyl Hydrocortisones: A New Series of Steroids with Enhanced Potency and Prolonged Action

Steroid chemists have recently developed a number of synthetic analogs of the adrenocortical steroids, several of which have been found to possess remarkable biological properties. The 9-α-halogen steroids developed by Fried and Sabo (*1*) have been found to possess a greater biologic potency than their nonhalogenated analogs with respect to all properties thus far studied. The sodium-retaining activity of these halogenated corticoids has been found to be enhanced out of proportion to the increase in "glucocorticoid" activities. The Δ-1 series of corticosteroids developed by Herzog *et al.* (*2*) have been found to possess greater biologic activity than their natural analogs with respect to properties dependent on the presence of an 11-oxygen group (for example, anti-inflammatory activity). On the other hand, those properties that do not depend on the presence of an 11-oxygen group (for example, sodium-retaining activity) have not been enhanced by the Δ-1 modification (*3*).

Very recently, the development of still another series—the 2-methyl analogs of

the corticosteroids—has been achieved by Hogg *et al.* (*4*). Byrnes and associates have found two of these steroids to be more potent than their nonmethylated analogs both in glycogen-depositing activity and in sodium-retaining activity as tested in the rat (*5*).

The present report (*6*) represents the initial use of these steroids in two additional species—man and the dog. We have studied in normal human subjects, in patients with Addison's disease, and in adrenalectomized dogs the comparative pharmacology of hydrocortisone (F), 2-methylhydrocortisone (methyl F), 9-α-fluorohydrocortisone (FF), and 2-methyl, 9-α-fluorohydrocortisone (methyl FF). In the dogs, additional observations were made on the effects of desoxycorticosterone (DOC) and aldosterone.

In human subjects, the oral administration of single doses of methyl FF (0.025 to 1.0 mg), FF (0.2 to 1.0 mg), methyl F (10 to 400 mg) and F (100 mg) induced retention of sodium and loss of potassium. More precise assays of these properties, performed in adrenalectomized dogs by a method previously reported (*7*), are summarized in Table 1. In brief, the 2-methyl compounds are many times more potent than their nonmethylated analogs. Methyl FF is seen to be more potent than aldosterone, and thus to be the most active sodium-retaining and potassium-losing steroid known at the present time.

The mechanism whereby the methylated steroids affect cation excretion was investigated in dogs. Methyl FF and, to a lesser degree, methyl F were capable of producing decreases in sodium excretion despite concomitant increases in glomerular filtration rate, indicating that these steroids increase the reabsorption of sodium by the renal tubules.

The decrease in circulating eosinophils that follows the administration of steroids may be used as one index of their "glucocorticoid" activity. Observations in both man and the dog indicated that the methylated steroids were only slightly more potent than the nonmethylated compounds during the first 4 hours following treatment. Eosinopenia persisted much longer, however, with use of the methylated steroids.

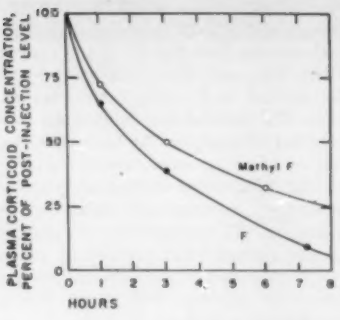

Fig. 1. Plasma 17,21-dihydroxy-20-ketosteroids (unconjugated) levels following intravenous injection of F and methyl F. The steroid concentration 10 minutes after injection is represented at "100-percent" concentration and "zero" hour. Curves are averages of three steroid tolerance tests in each of three subjects.

Whereas the direct biologic effects of a single oral dose of hydrocortisone ordinarily disappear in less than 24 hours, the effects of the 2-methyl derivatives were found to persist for approximately 48 hours in our studies in human subjects. Studies were accordingly designed to determine whether this prolonged action of the methylated steroids could be related to a slower rate of metabolic inactivation by the body.

Following administration of F and methyl F to human subjects, blood levels were determined at various intervals using a modification of the method of Silber and Porter (*8*) for measuring dichloromethane-soluble 17,21-dihydroxy-20-ketosteroids. It was consistently found that methyl F was removed from the circulation at a slower rate than F (Fig. 1). This was true whether the steroids were administered by vein or by mouth.

Following the administration of F to human subjects, one can account for approximately 30 percent of the administered dose by the determination of 17,21-dihydroxy-20-ketosteroids in the urine, using the method of Silber and Porter (*8*). The principal product thus measured is tetrahydrocortisone glucuronide. By way of contrast, following the administration of methyl F one can account for no more than approximately 5 percent of the administered dose using the same chemical methods.

It is suggested that the presence of the 2-methyl group alters the susceptibility of the steroid to enzymatic attack so that the processes by which F is metabolized operate less efficiently, and other processes assume greater prominence. As a result, removal of the methylated steroid from the circulation proceeds slowly, and during the metabolism of the steroid the 17,21-dihydroxy-20-keto configuration is lost. To some degree, the enhanced potency as well as the prolonged action of the 2-methyl steroids might be explained by the slower rate at which the body metabolizes them to inactive forms.

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Table 1. Relative effectiveness of various steroids on excretion of Na^+ and K^+ in the adrenalectomized dog, using DOC as a standard. The figures in parentheses represent 95-percent confidence limits. Ratios of potency are adjusted for molecular weight, and dosages are compared on an equimolar basis.

Steroid	Sodium		Potassium	
	Effect	Potency	Effect	Potency
DOC	Retention	1	Loss	1
Aldosterone	Retention	39 (26–61)	Loss	29 (20–41)
Methyl FF	Retention	49 (19–100)	Loss	155 (75–353)
FF	Variable		Loss	5.5 (3.1–10.7)
Methyl F	Variable		Loss	1.0 (0.5–2.1)
F	Loss		Loss	0.04 (0.026–0.063)

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2 December 1955

Oral Phosphatase Levels and Caries Activity

Oral phosphatases in human saliva are thought to be principally of bacterial cell origin (*1–4*) and in part of glandular origin (acid phosphatase from the parotid glands, *3*). The significance of these enzymes in saliva is not clear, yet correlations have been suggested between their titers and certain oral debilities (*5, 6, 7*).

Lactobacilli show little phosphatase activity (*2, 4*); however Bray and King (*8*) demonstrated high degrees of phosphatase activity in 14 groups of organisms that are commonly found in the oral environment. Fitzgerald (*4*) has suggested a possible caries-activity test based on the titer of phosphatases in saliva.

Our experiment (*9*) was conducted to determine a possible relationship between

Table 1. Statistical analysis of data obtained from phosphatase activity in the whole salivas of 26 caries-free and 26 caries-active persons.

Activity	Caries-free	Caries-active
*Alkaline**		
Range	0.06– 1.98	0.06– 1.98
Mean ($\bar{x}$)	0.58	0.68
S. D. (σ)	0.66	0.50
$\frac{\text{Dev.}}{\sigma} = \frac{\bar{x}_1 - \bar{x}_2 - O}{\sigma x_1 - x_2} = 0.61$		
*Acid**		
Range	0.90–12.60	2.40–13.80
Mean ($\bar{x}$)	5.65	7.61
S. D. (σ)	4.11	3.30
$\frac{\text{Dev.}}{\sigma} = \frac{\bar{x}_1 - \bar{x}_2 - C}{\sigma \bar{x}_1 - \bar{x}_2} = 1.9$		

* Units of phosphatase per 100 ml of whole saliva.

caries activity and phosphatases found in whole stimulated saliva. Analyses for both acid and alkaline phosphatase were performed on a randomly selected group and on caries-free and caries-active individuals.

Fifteen milliliters of paraffin-stimulated saliva were collected from each of 100 naval recruits ranging in age from 17 to 20 years. Acute cases of gingival infection were eliminated from this otherwise randomly selected group. Similar saliva samples were collected from 26 caries-free and 26 caries-active individuals who had had no dental restorations. The caries-free group was selected by clinical and radiographic examination. The caries-active individuals were selected clinically on the basis of the existence of ten or more carious lesions.

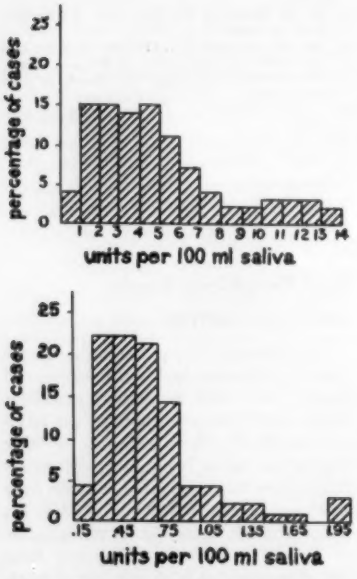

Fig. 1. Phosphatase activity in whole salivas of 100 randomly selected naval personnel of age ranging from 17 to 20 years. (Top) Acid pohsphatase: mean, 4.72; range, 0.60 to 13.8; standard deviation, ± 3. (Bottom) Alkaline phosphatase: mean, 0.57; range, 0.12 to 1.92; standard deviation, ± 0.405.

The colorimetric method of Seligman *et al.* (*10*), as adapted for saliva tests by Chauncey (*3*), was used for phosphatase determinations. The Coleman junior spectrophotometer at an optimum wavelength of 525 mμ and 10 by 75-mm cuvettes were used.

The mean acid phosphatase activity in whole salivas of 100 randomly selected persons was 4.72 units/100 ml, while that for alkaline phosphatase was 0.57 units/100 ml (Fig. 1). The mean acid and alkaline phosphatase activities in whole salivas of 26 caries-free individuals were 5.65 units/100 ml and 0.58 units/100 ml, respectively. The caries-active group showed mean phosphatase activities of 7.61 units/100 ml (acid) and 0.68 units/100 ml (alkaline).

Statistical analysis of the differences in the mean acid and alkaline phosphatase levels for caries-free and caries-active groups did not reveal significance. The probability of obtaining the observed differences in the means for acid phosphatase was 7 percent or less; for alkaline phosphatase, it was 54 percent or less (Table 1).

That oral phosphatases are predominately of bacterial cell origin seems well established (*1–4*). Rosebury (*6*) and others (*4, 7*) have ascribed possible roles to phosphatases in saliva that are based solely on known activity characteristics of these enzymes isolated from other tissues (bone, liver, kidney, serum, and so forth). The mere existence of a phosphatase associated with the bacterial cell does not, however, preclude the action of this enzyme according to previously accepted theory. Thus it becomes important to look on the oral phosphatases as entities and to characterize them according to the specific oral debility in which they are suspected to be taking part. For instance, recent tests in this laboratory showed that acid phosphatase of the parotid secretion was inhibited by tartrate, which has been shown to inhibit prostatic phosphatase (*11*). This would immediately bring to mind specific correlations regarding tests for cancer of prostate gland. However, characterizations of both parotid and prostatic enzymes become essential before conclusions may be drawn.

The failure to correlate the presence of phosphatases in saliva with certain oral debilities (dental caries, calculus formation, periodontal disease, and so forth) probably results from the fact that these enzymes are present in so many of the organisms normally present in the mouth that any association is obscured.

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25 August 1955

Possible Function of Serum Proteins in Tissue Culture

In a recent article by Eagle (*1*) it was found that, with the exception of the necessity of serum proteins, completely defined chemical media are possible that support both growth and multiplication in certain lines of mammalian cells. The possibility that the serum proteins contribute as yet undetected trace elements or vitamins is being investigated by him (*1*, p. 503).

Although the presence of such trace elements or vitamins is certainly a possibility, there is another alternative that I feel should be considered. Both from the work described and what is known about protein chemistry and function, it seems that the essential substances could be proteins, perhaps certain of the serum proteins themselves.

From the results given in the paper (*1*, p. 503) it appears that the activities of the protein fractions were determined by the extent to which denaturation could not occur in the fractionation procedure. Exhaustive dialysis would remove most of the salts and other impurities, and this is known to render many proteins unstable and susceptible to structural changes (*2*, pp. 211–213; *3*). Alcohol is a denaturing agent for many proteins (*2*, p. 207; *4*, p. 173), and

there is evidence that serum proteins resulting from alcohol fractionation are denatured to the extent that, although still soluble, they are poorly metabolized when they are injected into an animal (*4*, pp. 460–461). Only the salting out method by the use of neutral salts is thought to leave the protein fractions in their native, unaltered form (*4*, p. 173) and apparently only by this method was Eagle able to obtain fractions that were consistent in their activity.

The possibility that specific proteins are essential for the activities of at least some mammalian cells would also seem compatible with some of the properties and roles that have been described for certain proteins. They could act on the cell membrane and affect its permeability to other materials. There is evidence that the protein hormone insulin acts in this way (*5*). There is good evidence that certain plasma proteins can enter cells fairly readily (*6*); and, once inside the cell, the essential protein may act by complexing smaller compounds whose activity may depend on this action. The tremendous importance of this property of proteins and the dependance of the biological function of many compounds on the alteration of properties resulting from such complex formation has been pointed out in detail by Needham (*7*). It seems to be an accepted fact that protein hormones somehow alter the metabolism of the cells they affect; and, because some proteins are present in relative abundance, this should not in itself rule out an essential metabolic role for them.

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22 November 1955

Early Man and Fossil Bison

At certain sites in and near the Great Plains, there are associations of fossil bison and early types of projectile points. Correlating these associations, I have developed a possible sequence of certain projectile points and of contemporaneous fossil bison forms (Fig. 1) (*1*).

In 1947, Skinner and Kaisen enumerated the known localities where fossil bison are represented (*2*). At a number of these localities, Folsom, Plainview, and Scottsbluff points have been found. Since 1947, Scottsbluff points have also been identified at the Finley site in association with *Bison* (*Bison*) *occidentalis* (*3*).

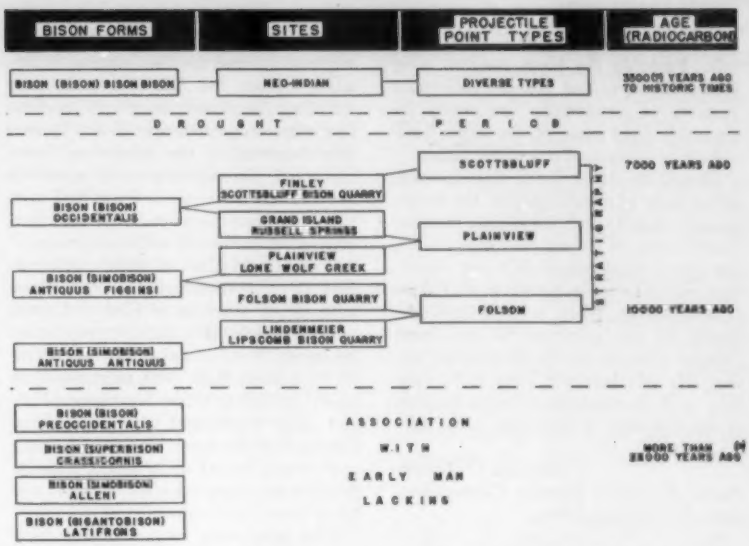

Fig. 1. Associations of bison forms with sites and projectile point types in the Great Plains.

Excavations at the MacHaffie site revealed that the Folsom complex is older than the Scottsbluff (*4*). This fact has been confirmed elsewhere by radiocarbon dates on a Folsom site (9883 ± 350 years ago) and on a Scottsbluff site (6876 ± 250 years ago)—dates that indicate an age difference of some 3000 years (*5*).

The Folsom-Scottsbluff succession having been established, it is evident that Fig. 1 shows the best possible way of correlating the fossil bison and projectile points.

The number of sites with associations will have to be increased before the results of the correlation can be regarded as established fact. Nevertheless, until contradictory evidence comes to light, it provides a working hypothesis.

Sound contradictory evidence is lacking. At the Lime Creek site, a Scottsbluff layer was reportedly found stratigraphically below a layer attributed to the Plainview complex (*6*). However, according to Krieger (who originally conceptualized the Plainview point), the Lime Creek specimens are not Plainview (*7*).

Plainview points may prove to be younger than Scottsbluff on the basis of a supposed geologic relationship between the Lime Creek site, with its Scottsbluff layer, and the nearby Red Smoke site, where authentic Plainview points were found. The geologic evidence, however, has not yet been published in a convincing manner.

One potential flaw in the chain of evidence must be noted. The points from Grand Island and Russell Springs are not typical Plainview points. Probably they are merely variants of the Plainview type. At the Red Smoke site, these so-called Meserve points were found in the same cultural layer as typical Plainview points.

Early man (Paleo-Indian) occupations appear to be separated from the later (Neo-Indian) occupations of the plains by a drouth period of some 3000 years, beginning about 6500 to 7000 years ago. Fossil forms of bison have not yet been found in any of the known Neo-Indian sites. And, with one possible exception, modern bison have not been found in sites attributed to early man on the Great Plains.

The possible exception is the Agate Basin site in Wyoming (*8*). There, the bison (said to be of historic species) were not classified according to the system Skinner and Kaisen developed. Unfortunately, they were discarded from the U.S. National Museum because they appeared to be only a superfluous addition to an already adequate collection of modern bison (*9*).

A renewed excavation of this site and a reexamination of its bison remains will show whether or not the historic species lived contemporaneously with *occidentalis* in the Paleo-Indian period. Contemporaneity seems to be out of the question, because the historic plains

bison of the Neo-Indian period is thought to have evolved gradually from *occidentalis*. Probably the bison remains were incorrectly identified. Smaller individual variants of *occidentalis* are nearly inseparable from some of the larger individuals of plains and woodland bison.

Should the Agate Basin bison remains prove to be of a fossil species, the archeologist, when he finds fossil bison remains (particularly of the *antiquus* subspecies), can assert with reason that any associated cultural remains belong to the Paleo-Indian period. When modern bison are found, he can attribute the associated cultural remains to the Neo-Indian period. He will however, have to be cautious with *occidentalis* remains because of the similarity of this form to the surviving race.

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29 August 1955

Quantitative Infrared Spectroscopy of Desoxyribonucleic Acid in the Fractional Milligram Range

Since desoxyribonucleic acid (DNA) is generally considered as the material from which genes are made, its characteristic infrared spectrum is of great biological interest (*1, 2*). Because of the very slight solubility of DNA in any but aqueous solvents and the rather strong absorption of infrared rays by water, it is desirable to examine the material in the solid state. However, the solid preparations of DNA, such as powders, films, or Nujol pastes, that are used for this purpose require relatively large amounts of substance and give only qualitative spectroscopic data at best.

This paper (*3*) describes quantitative infrared spectroscopy of DNA in the fractional milligram range with use of suspensions in solid KBr, which is very transparent to infrared, for specimen preparation and a condensed infrared beam for spectroscopic examination. The technique developed for this purpose principally follows the KBr-disk procedures that have been used mainly for qualitative infrared spectroscopy (*4–6*). Various improvements of the procedure, especially of the technique of specimen preparation, however, have enabled us to carry out quantitative infrared spectrometry in the fractional milligram range.

Aqueous solutions of highly polymerized DNA (Worthington) were mixed with dilute solutions of KBr of highest purity (Merck-Darmstadt) to give exact amounts (20 to 300 μg) of DNA in 10 ml of 1.2-percent KBr. The mixtures were frozen quickly in a Dry Ice-acetone bath and then lyophilized with a modified cryochem freeze dryer. The freeze-drying cycle lasted for 24 to 30 hours, and the drying was completed at 25° to 30°C and 30 to 90 μ-Hg pressure.

Fifty milligrams of the frozen, dried material was transferred into a steel die of ¼-in. diameter. The die was evacuated to about 1 mm-Hg and transparent disks of 1-mm thickness were pressed with a Carver press. The optimum time of pressing was 1 minute. The optimum pressure corresponded to the reading of 8000 lb/in.^{2} on the Carver press gage. Single or double plunger dies were used. The single plunger dies had to be greased with a minute quantity of graphite in order to prevent cracks when the disks were pressed out. The double plunger die was relativly simple to use and allowed pressing of disks of almost identical weights (50 mg) and thicknesses (1 mm).

Infrared spectroscopy was carried out with a Beckman I.R. 2 spectrometer that was equipped with a beam-condensing unit comprised of a system of silver chloride lenses. The disk was inserted in a disk holder, focused in the condensed beam, and examined spectroscopically. Measurement of bands was carried out by the conventional base-line method.

The infrared spectra of the disks given in Fig. 1 show all the characteristic vibrations of DNA that have previously been observed in the powders, films, or pastes. Many important vibrations, such as the weak band at 9.80 μ, which is present in DNA but absent in ribonucleic acid, appear at least as clear or clearer in the disk spectrum from less than 50 μg DNA than they were found in the spectra from powders, films, or pastes requiring 20 times more material.

The evaluation of our method for quantitative infrared spectrometry of small amounts of DNA was carried out in disks containing 9, 18, 27, 36, 54, and 72 μg of DNA. Three different absorption bands—namely, the bands at about 8.1 μ, 9.80 μ, and 10.30 μ—were examined in each disk, and the absorbancies found with the base-line method were plotted versus concentrations (Fig. 2).

Figure 2 demonstrates the linearity of the function of absorbancy versus concentration found in all the three absorption bands and indicates strict observance of Beer's law at even low DNA concentrations. Furthermore, the linearity of these functions is shown by agreement of the three extinction coefficients that were calculated from the experimental data. At DNA concentrations of 36 μg and above, extinction coefficients for all the three bands show percent average deviations of ±3 to ±4.2 percent. At DNA concentrations below 36 μg, the deviations increase in the two weaker bands (9.80 μ and 10.30 μ). In the strongest band (8.1 μ), however, the percent average deviation of the extinction coefficients remains at ±3 percent even at DNA concentration as low as 18 μg.

It is believed that the method for quantitative infrared spectrometry of small

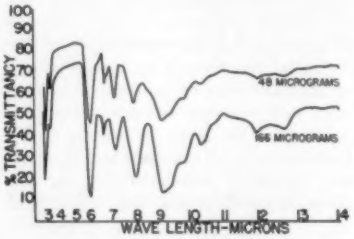

Fig. 1. Infrared spectra of desoxyribonucleic acid suspended in solid potassium bromide. The upper curve gives the transmittancy of a disk, containing 48 μg of DNA in 50 mg of KBr; the lower curve gives the transmittancy of a disk containing 166 μg of DNA in 50 mg of KBr.

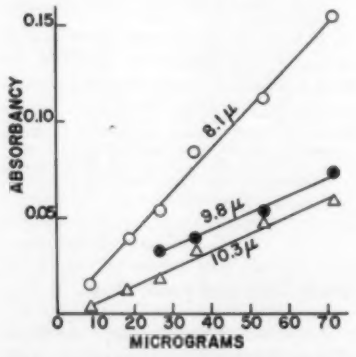

Fig. 2. Graphic indication of infrared absorbancy versus concentration of DNA in disks containing 9, 18, 27, 36, 54 and 72 μg of DNA. The upper curve was obtained from measurements of the bands at 8.1 μ, the middle curve from the absorbancies of the bands at 9.80 μ, and the bottom curve from those of the bands at 10.30 μ.

amounts of DNA shown in this paper will be important for biological and structural studies and that further experiments with smaller dies will permit infrared analysis of even smaller quantities.

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8 August 1955

Directional Differences in Pigeon Homing

The results of pigeon homing investigations made at the Max-Planck-Institut at Wilhelmshaven were the first to suggest a directional difference in orientation. The data from a number of releases showed a definite superiority of the homing results when the pigeons were taken south for release compared with the results when they were taken east. This was true for distances as short as 15 mi, but it was also true for 100 and more mi. Results from north and west releases were not available for a direct comparison.

Further work was done in the Carolinas (*1*). To collect data bearing more explicitly on the question, we made pigeon releases simultaneously from four points north, east, south, and west of the loft. Releases of single birds were made at each point of the "cross" release pattern at intervals of 10 min. Observers at the loft recorded the time of arrival of each bird. In the present report, we base the comparison of performance from the four directions of flight entirely on homing success.

A series of 12 cross releases was made with birds from two different lofts in the Durham region. In November 1954, pigeons from a loft located in the Duke Forest were flown twice at a distance of 16 mi and a third time at a distance of 53 to 60 mi. Birds from a second loft, which was located on the edge of Durham, were used in the period from February to April 1955 in a series of eight cross releases at 17¼ mi and in a ninth release from 53 to 59 mi (*2*). In the 16- to 17-mi flights, we selected release points that would provide a symmetrical cross pattern of release points and therefore could not choose places that were suitable for observing departure orientation. Forestry lookout towers were used as release points for the 53- to 60-mi flights; the cross pattern was not perfectly symmetrical. However, the distances for the flights from the north and from the south remained equal.

Within each series, the intervals between releases varied from 3 to 15 days; the same birds were used repeatedly, new ones being introduced to replace losses. On successive release days, the direction of displacement of individual birds was shifted to limit practice effects. In the series of releases at 17¼ mi, the whole groups were shifted, the sequence for the birds that were first displaced to the north being N, E, W, S, N, S, E, W; the others were rotated in step with these. For the other releases, new groups were formed—for example, birds that had last been sent north were assigned equally to groups that were to be taken E, S, and W. About half the birds were inexperienced in that they had never been removed forcibly from the loft area before they were used in the cross releases; the remainder had received a few previous homing releases from various directions. For their first cross release, the birds were always assigned to a group going in a different direction from that of their immediately preceding displacement.

Despite the 10-min release interval between birds, flight pairs or larger groups were formed on the way home in some cases. To meet the requirement of statistical independence in the data, we have considered only those birds that arrived singly and the fastest member of each group in the analysis of the results. The cross releases provided homing records for 558 of the short-distance flights and for 117 of the 53- to 60-mi flights. These were approximately equally distributed at each distance among the four directions. Figure 1 summarizes the homing performances for both distances separately. Birds displaced to the south yielded a relatively larger number of returns at 15 mi/hr or faster. Likewise, flights from the south showed a remarkably low number of losses. Birds displaced to the north, on the other hand, made the smallest number of quick returns and showed by far the largest number of losses. Chi-square tests of the data in Fig. 1 show significant departures from the distribution expected by random sampling (*3*). The winds, which averaged about 8 mi/hr and were most often from the west, did not appreciably affect the results. Flights from the north were slightly favored over those from the south by the average wind direction.

The fact that directional differences are found at only 16 to 17 mi strongly suggests that even at this short distance orientation is not primarily based on landmarks. Sheer landmark orientation or random searching should result in comparable homing performance from all directions. However, even with the practice afforded by eight flights from the 17¼-mi distance (twice from each point for each group), the north-south contrast in homing apparently was not erased (*4*).

There is no reasonable ground for doubting that a south-to-north superiority of homing exists in these birds as far as these two loft locations are concerned. It should be noted that the two Durham lofts are situated 2.6 mi apart, which makes it unlikely that individual features of the loft site are responsible for the observed effect. Since further work is

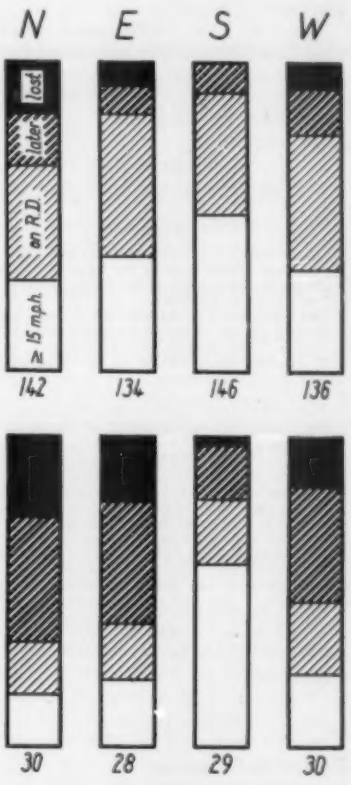

Fig. 1. Percentage differences in homing success dependent on displacement directions (indicated on top). (Top) 16 to 17¼ mi; (bottom) 53 to 60 mi. The figures beneath the columns show the number of independent flights. Legend: (white) percentage of returns at 15 mi/hr or faster; (fine hatching) percentage of returns slower than 15 mi/hr but within release day; (heavy hatching) percentage of returns on subsequent days; (black) percentage of birds lost.

planned to test birds of the same and of different stocks at other home points, we must reserve judgment regarding the prevalence and consistency of the directional factor in homing until more results are available. Already, parallel data have been obtained at a loft in Mountville, S.C. (*5*) and in southern Germany; data from both points suggest that directional differences are a general phenomenon in pigeon homing. The combined data of these cross releases thus clearly confirm the earlier Wilhelmshaven findings of systematically unequal homing performances from different directions.

We are not able at this time to offer an explanation of the direction differences. However, it is conceivable that this discovery may provide a clue to the basis of the bird's orientation ability. Further study of the effect seems imperative.

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1. These experiments were conducted under contract NR 160-244 between the Office of Naval Research, Department of the Navy, Washington, and Duke University.
2. We are indebted to the following for their assistance in the 53- to 59-mi release: M. H. Carson, T. H. Goldsmith, L. C. Graue, T. N. E. Greville, D. R. Griffin, H. B. Hitchcock, and G. V. T. Matthews.
3. For the 16- to 17-mi flights, $\chi^2 = 38.6$ (9 d.f.); $P = < 0.0001$. For the 53- to 60-mi flights, testing returns from each direction on the release day versus later and lost birds yields $\chi^2 = 14.8$ (3 d.f.); $P = 0.002$. For both distances combined $\chi^2 = 51.5$ (9 d.f.); $P = < 0.000001$.
4. Comparing independent flights from N and S from a total of 38 birds that flew in all eight releases at 17¼ mi gives the following ratio of ≥ 15 mi/hr to < 15 mi/hr birds: (i) during the first four releases, 5/19 and 16/17 ($\chi^2 = 4.57$, 1 d.f.; $P = 0.032$); (ii) during the second four releases, 11/20 and 19/12 ($\chi^2 = 4.13$, 1 d.f.; $P = 0.042$). Thus, the only obvious effect of practice is a general increase in speed.
5. We are indebted to John B. Cooley for providing birds and assistance in these experiments.

29 August 1955

Formation Constants for Cu(II)-Peat Complexes

A great deal of evidence, much of it indirect, points to the fact that soil organic matter forms relatively stable complexes with di- and trivalent metal ions. However, no quantitative information concerning the stability of such complexes is available. This is a preliminary report (*1*) on the determination of formation constants for metal ion-organic matter complexes; it deals entirely with the binding of Cu(II) by peat.

Table 1. Ionization constants of H-peat and formation constants of Cu(II)-peat complexes.

Cu(II) added (10^3 mole/lit)	KNO_3 (mole/lit)	*pka*	*n*	*Kc* ($\times 10^{-6}$)	*B*
2	0.01	5.5	2.2	80	2.5
2	0.1	4.8	2.2	8.0	2.5
2	1.0	4.3	2.2	1.6	2.5
0.6	1.0	4.3	2.2	1.0	
0.2	1.0	4.3	2.2	1.0	

Peat and other soil organic matter specimens possess acidic (proton-donating) groups thought to be carboxylic, phenolic, and enolic (*2*). Such groups are believed to be responsible for the cation exchange capacity, which generally lies between 2 and 3 milliequivalents per gram. The intrinsic ionization constant for the carboxylic groups appears to be about 10^{-5} (*3*), and these are the only acidic groups thought to be ionized to an appreciable extent at *p*H of 7 and below.

The similarity of the acidic nature of peat to that of polyacrylic acid and the various cross-linked polymers whose Cu(II) complexes were studied by Gregor *et al.* (*4, 5*) suggested that a similar treatment might yield values for the formation constants of Cu-peat complexes.

The peat-Cu(II) reaction may be written in two ways, with P referring to the concentration of peat functional groups:

$$2P^- + Cu^{++} \leftrightarrows CuP_2;$$

$$Kc = \frac{(CuP_2)}{(Cu^{++})\,(P^-)^2} \qquad (1)$$

$$2HP + Cu^{++} \rightleftarrows CuP_2 + 2H^+;$$

$$B = \frac{(CuP_2)\,(H^+)^2}{(Cu^{++})\,(HP)^2} \qquad (2)$$

For calculating the apparent formation constant *Kc* the condition is sought where $CuP_2 = Cu^{++}$—that is, where the degree of formation is 0.5 (*6*). Then $Kc = 1/(P^-)^2$.

As is pointed out by Gregor *et al.* (*4*), since *Kc* is a constant for a reaction between a metal ion and charges on a colloidal particle, *Kc* should vary with the degree of neutralization and the ionic strength to the same extent as the acid ionization constant but in the opposite direction. On the other hand, *B*, which essentially is the product of *Kc* and the ionization constant *ka*, should be independent of ionic strength.

To evaluate Eqs. 1 and 2 for Cu(II)-peat complexes, 0.2 g (0.46 milliequivalents of acidic groups) of acid-washed Florida peat was shaken for 48 hours with 50 ml of solutions containing 0.2, 0.1, 0.06, or 0.02 mmole of $Cu(NO_3)_2$ and 0 to 0.35 milliequivalents of NaOH. The systems containing 0.1 mmole of Cu(II) were 0.01, 0.1 or 1*N* in KNO_3; the systems containing the other amounts of Cu(II) were 1*N* in KNO_3.

The *p*H's were measured with glass and calomel electrodes. Titration curves for the acid-washed peat and for the systems containing 0.02, 0.06, and 0.2 mmole of Cu(II) are shown in Fig. 1. Strong binding of Cu(II) is indicated by the displacement of the curves.

The *p*H's of the partially neutralized peats at the three salt concentrations were plotted against log $(1-\alpha/\alpha)$, where α is the degree of neutralization calculated from the amount of base required to raise the *p*H to 7 in 1*N* KNO_3. The points for each salt concentration were fitted to a straight line, leading to the values for *pka* (the negative logarithm of the acid ionization constant) and *n* listed in Table 1. From the derived equations relating the extent of ionization with *p*H and from the condition of electroneutrality, values for CuP_2, P^- and H^+/HP were calculated. No corrections for activity coefficients were attempted.

To determine values for *Kc* and *B*, $\bar{n}$, the average number of acid groups bound for each Cu(II) ion in the system, was plotted against *p*P (the negative logarithm of the concentration of ionized peat) or log (H^+/HP). The former yielded values of *Kc* (log Kc = 2*p*P at $\bar{n} = 0.5$) that varied widely with salt concentration. The "corrected" constant *B* was independent of salt concentration in the range studied. Values for *Kc* and *B* are listed in Table 1.

The Cu-peat systems were filtered, and Cu(II) was determined in the decolorized filtrates (darco carbon) with diethyldithiocarbamate. The mean of the formation constants (*Kc*) calculated from analytic Cu(II) data and the electroneutrality condition was 3.2×10^6, which is in reasonable agreement with the value deduced from the titration data.

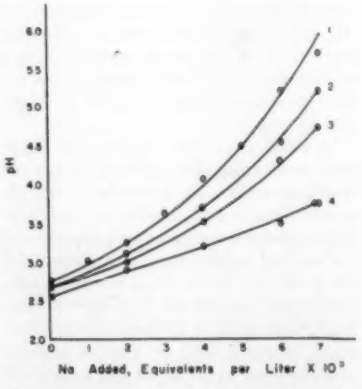

Fig. 1. Neutralization curves of 0.0092*N* H-Peat in 1*M* KNO_3 (1) no Cu(II); (2) 0.0002*M* Cu(II); (3) 0.0012*M* Cu(II); (4) 0.004*M* Cu(II).

The stability of the Cu-peat complex, particularly at low salt concentrations, would result in extremely small quantities of soluble ionic Cu(II) in most soils.

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16 August 1955

Modification of Electric Activity in Cochlear Nucleus during "Attention" in Unanesthetized Cats

Attention involves the selective awareness of certain sensory messages with the simultaneous suppression of others. Our sense organs are activated by a great variety of sensory stimuli, but relatively few evoke conscious sensation at any given moment. It is common experience that there is a pronounced reduction of extraneous sensory awareness when our attention is concentrated on some particular matter. During the attentive state, it seems as though the brain integrates for consciousness only a limited amount of sensory information, specifically, those impulses concerned with the object of attention.

An interference with impulses initiated by sensory stimuli other than those pertaining to the subject of attention seems to be an obvious possibility. It is clear that this afferent blockade might occur at any point along the classical sensory pathways from receptors to the cortical receiving areas, or else perhaps in the recently disclosed extraclassical sensory paths that traverse the brain-stem reticular system (*1*).

Recent evidence indicates the existence of central mechanisms that regulate sensory transmission. It has been shown that appropriate stimulation of the brain-stem reticular system will inhibit afferent conduction between the first- and second-order neurons in all three principal somatic paths (*2–4*). During central anesthesia, the afferent-evoked potentials in the first sensory relays are enhanced. This appears to be due to the release of a tonic descending inhibitory influence that operates during wakefulness and requires the functional integrity of the brain-stem reticular formation.

The possibility that a selective central inhibitory mechanism might operate during attention for filtering sensory impulses was tested by studying (*5*) afferent transmission in the second- or third-order neurons of the auditory pathway (cochlear nucleus) in unanesthetized, unrestrained cats during experimentally elicited attentive behavior. Bipolar stainless steel electrodes with a total diameter of 0.5 mm were implanted stereotaxically in the dorsal cochlear nucleus through a small hole bored in the skull. The electrode was fixed to the skull with dental cement. A minimum of 1 week elapsed between the operation and the first electroencephalographic recordings. Electric impulses in the form of short bursts of rectangular waves (0.01 to 0.02 sec) at a frequency of 1000 to 5000 cy/sec were delivered to a loudspeaker near the cats at an intensity comfortable to human observers in the same environment.

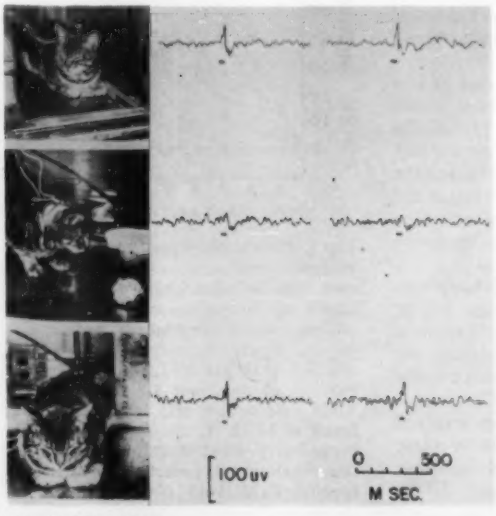

Fig. 1. Direct recording of click responses in the cochlear nucleus during three periods; the photographs were taken simultaneously. (Top and bottom) Cat is relaxed; the click responses are large. (Middle) While the cat is visually attentive to the mice in the jar, the click responses are diminished in amplitude.

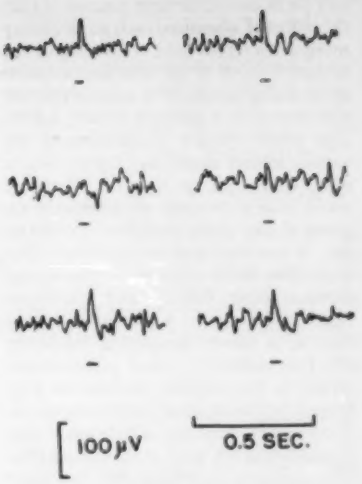

Fig. 2. Click responses recorded from the cochlear nucleus of the cat. (Top) cat is relaxed; (middle) cat is attentively sniffing an olfactory stimulus; (bottom) cat is relaxed again. Note the reduced amplitude of the click responses when the animal is sniffing.

Three types of sensory modalities were used to attract the animal's attention: visual, olfactory, and somatic. As is illustrated in Fig. 1, during presentation of visual stimuli (two mice in a closed bottle), the auditory responses in the cochlear nucleus were greatly reduced in comparison with the control responses; they were practically abolished as long as the visual stimuli elicited behavioral evidence of attention. When the mice were removed, the auditory responses returned to the same order of magnitude as the initial controls. An olfactory stimulus that attracted the animal's attention produced a similar blocking effect. While the cat was attentively sniffing tubing through which fish odors were being delivered, the auditory potential in the cochlear nucleus was practically absent (Fig. 2). After the stimulus had been removed and when the cat appeared to be relaxed once more, the auditorily evoked responses in the cochlear nucleus were of the same magnitude as they had been prior to the olfactory stimulation. Similarly, a nociceptive shock delivered to the forepaw of the cat—a shock that apparently distracted the animal's attention—resulted in marked reduction of auditorily evoked responses in the cochlear nucleus.

If this sensory inhibition during attentive behavior, as demonstrated in the auditory pathway, occurs in all other sen-

sory paths except the ones concerned with the object of attention, such an inhibitory mechanism might lead to favoring of the attended object by the selective exclusion of incoming signals. It is conceivable not only that such a selective sensory inhibition might operate simultaneously for various sensory modalities, leaving one or more unaffected but that the selectivity could extend to some discriminable aspects of any single modality—for example, to one tone and not to others. This suggestion finds support in the recent demonstration that sensory "habituation" may occur to a particular tone—that is, a slowly developing inhibitory effect on auditorily evoked potentials observed in the cochlear nucleus on prolonged repetition of a given tone, an influence that does not affect other frequencies that are novel to the animal (*6*). The pathway by which this inhibitory influence acts on incoming auditory impulses remains to be determined, but experiments now in progress have shown that during electric stimulation of the midbrain reticular formation, the auditory potential in the cochlear nucleus is depressed (*7*).

The present observations suggest that the blocking of afferent impulses in the lower portions of a sensory path may be a mechanism whereby sensory stimuli out of the scope of attention can be markedly reduced while they are still in their trajectory toward higher levels of the central nervous system. This central inhibitory mechanism may, therefore, play an important role in selective exclusion of sensory messages along their passage toward mechanisms of perception and consciousness. In a recent symposium on brain mechanisms and consciousness, Adrian pointed out that "the signals from the sense organs must be treated differently when we attend to them and when we do not, and if we could decide where and how the divergence arises we should be nearer to understanding how the level of consciousness is reached" (*8*).

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25 August 1955

Effect of Barbiturates on Acetylation

Several different groups of investigators have recently attempted to demonstrate a biochemical action of barbiturates and other central nervous system depressants. After McLennan and Elliott (*1*) showed that acetylcholine synthesis by brain slices was inhibited by these agents, interest focused on the study of acetylation reactions generally, either in tissue slices or in relatively purified enzyme systems. The results of these studies, however, have been distinctly at variance with one another so that it has not been possible to draw any clear conclusions other than that the experimental methods offered some unseen difficulties (*2–4*). Experiments carried out in this laboratory may shed some light on this problem.

The acetylation system that was studied was that described by Kaplan and Lipmann—namely, the acetylation of arylamines by a pigeon liver enzyme in the presence of adenosine triphosphate (ATP) and coenzyme A (coA) (*5*). Both the crude coA and purified coA were used (Nutritional Biochemicals and Pabst Laboratories, 300 units/mg, 75 percent pure). The analytic procedure for sulfanilamide was that of Bratton and Marshall (*6*), using a photoelectric colorimeter. Similar results were obtained from the use of the pure and the crude coA preparations.

Purified coA was stable when it was kept cold and dry, but aqueous solutions rapidly lost their activity, presumably through oxidation. By dissolving the coA in 1.0*M* cysteine at *p*H 6.8, flushing the vessel with nitrogen, and storing in the freezing chamber of a refrigerator, it was possible to keep the coA solution active for 1 to 2 weeks.

The effect of various barbiturates on this "pure" acetylating system can be seen in Fig. 1. All the barbituric acid derivatives used inhibit acetylation, the amount of inhibition being related to the concentration of the drugs. The concentrations used included the range achieved pharmacologically in the use of these agents as anesthetics. One of the drugs was a convulsant barbiturate, 1,3-dimethylbutyl barbituric acid (*7*), and it too inhibits acetylation. Also tested were MC 1415 (2,2-diethyl-1,3-propanediol) and MC 2973 (2,2-diethyl-1,4-butanediol (*8*). Neither of these substances produces any significant inhibition of acetylation.

With respect to the mechanism of inhibition, addition of extra purified coA will alleviate the inhibition, but addition of extra ATP to the incubating mixture will not (Table 1). Addition of magnesium ions increases the inhibition by barbiturates rather markedly, perhaps by activating some residual ATPase, which may still contaminate the enzyme preparation. When the enzyme system from liver is further fractionated, it has been shown that it is stimulated, rather than inhibited, by magnesium (*9*).

The results presented, in agreement

Table 1. Effect of coA and ATP on inhibition of acetylation by phenobarbital.

coA (units)	ATP (μmole)	Phenobarbital ($10^{-3}M$)	Acetylation (%)	Inhibition (%)
Experiment 1				
0	4	0	0	
1.5	4	0	64.8	
1.5	4	1	50.0	22.8
3.0	4	0	75.1	
3.0	4	1	73.6	2.0
Experiment 2				
0	4	0	0	
1.5	4	0	70.8	
1.5	4	5	41.6	41.2
1.5	8	5	38.0	46.3

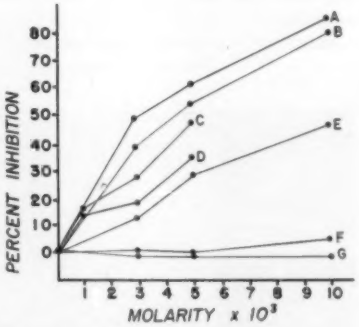

Fig. 1. Each value represents the average of duplicate determinations. Contents of each tube included 4 μmole of ATP, 0.4 μmole of sulfanilamide, 25 μmole of sodium acetate, 20 μmole of sodium citrate, 10 μmole of cysteine, 150 μmole of tris buffer at *p*H 8.3, 0.25 ml of aged enzyme solution, and 1.2 units of coA. Total volume 1.0 ml; incubated for 2 hours at 37°C. *A*, thiopental; *B*, 1,3-dimethylbutyl ethyl barbituric acid; *C*, phenobarbital; *D*, pentobarbital; *E*, amobarbital; *F*, MC1415; *G*, MC2973.

with the views of Govier and Gibbon (*3*), support the idea that barbiturates may produce their effects by interfering with the activation of acetate and consequently the acetylation of choline. The active site in the barbiturate molecule may reside in the "urea" portion, as evidenced by the lack of any effect of the two nitrogen-free substances tested.

The contradiction of the results of Mendelson and Grenell (*4*) remains unexplained. Their procedure was very similar to that used here, the major difference being that the present results were obtained by using a somewhat more than half-activated system.

In summary, a series of barbituric acid derivatives has been shown to produce inhibition of acetylation in a relatively "pure" acetylating system. A convulsant barbiturate also produces marked inhibition, but compounds that might be considered as "urea-free" depressants and convulsants (*10*), respectively, do not produce significant inhibition. Inhibition produced by phenobarbital could be relieved by addition of extra coA, but was not found to be relieved by addition of ATP.

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* With the technical assistance of Robert McCoy.

6 September 1955

Color Autoradiography

Although the effect of radioisotopes on ordinary photographic emulsion is well known, there are no reports on results obtained with color film. It occurred to us that multilayer color film is, in effect, a stack of absorbers that should yield, after photographic development, a hue dependent on the ratio of absorption in the layers. This ratio should be a function of the energy spectrum of emitted radiation, and hence each radioisotope should produce a specific hue. Furthermore, the amount of radiation from a given isotope absorbed by the film should affect only the brightness but not the hue of the final product. The present study bears out these considerations and indicates that color-film autoradiography is practicable (*1*).

Table 1. Effect of radioisotopes on color film.

Isotope	$E_{max.}$* (Mev)	Trials (No.)	Munsell color No. (mean ± S.D.†)	Actual color range ± 1 S.D.†
Carbon-14	0.16	12	68.5 ± 4.7	Bluish, blue-purple to blue
Sulfur-35	0.17	16	64.4 ± 3.1	Purplish, blue to greenish blue
Calcium-45	0.25	8	51.9 ± 5.5	Bluish, blue-green to bluish green
Iodine-131	0.60‡	23	46.3 ± 10.6	Bluish, blue-green to greenish green-yellow
Phosphorus-32	1.7	8	35.9 ± 1.2	Greenish, green-yellow to green-yellow

* Values for $E_{max.}$ were obtained from *Isotopes* (Oak Ridge National Laboratory, Oak Ridge, Tenn., 1954). † Standard deviation. ‡ Most abundant β.

One-inch diameter filter paper disks (Whatman No. 1) were dipped into solutions of P^{32}, I^{131}, Ca^{45}, S^{35}, and C^{14} ($25–25 \times 10^{-5}$ μc/ml) and air-dried. Approximately 0.08 ml was absorbed per paper in this manner. The disks were pressed against the emulsion side of Ektachrome film (Eastman Kodak Company, daylight type), and the film was exposed from 1 to 40 days. Photographic development followed the manufacturer's recommendations (*2*). Classification of the resultant hues was made by visual comparison with Munsell color standards (*3*).

Table 1 lists the characteristic hue produced by each isotope. The range of color encompassed the blues for the least energetic particles to the green-yellows for the most energetic. The usable range appeared to be 10^7 to 10^{10} total disintegrations per square centimeter. Within this range, the characteristic hue for each isotope remained constant, regardless of the density of the image. It is interesting that thin absorbers (cellulose tape, 9 mg/cm²), when they were placed between the source and the film, produced an increased density with no appreciable change in hue. In the case of I^{131}, which emits both β and γ rays, the hue indicates that the former radiation was primarily responsible for exposing the film.

From these experiments, it is evident that color autoradiography will permit differentiation of isotopes, provided that sufficient difference exists between energy spectra. For example, a mixture of inorganic I^{131} and C^{14}-tyrosine was separated chromatographically on paper and identified by this technique.

Other possible applications for color autoradiography may be (i) demonstration of isotope emitter characteristics, (ii) determination of proportions of two or more isotopes in a mixture, and (iii) improvement of image detail in autoradiography of tissues. Of course, the value of such results must depend on the type of film that is available. The film used in these studies permitted only a limited approach to these applications. Furthermore, the complex method of photographic development is a decided deterrent to the use of color film as compared with standard film. Perhaps the introduction of special types of multilayered emulsions might make color autoradiography a valuable and convenient tool for the laboratory.

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References and Notes

1. An excellent discussion of the color film used in this study appears in *Kodak Color Handbook* (Eastman Kodak Co., Rochester, N.Y., 1953).
2. We are indebted to Kenneth S. Carnes and Earl E. Powers of the Medical Illustration Laboratory of this hospital for processing the film.
3. In the Munsell system, the complete visual color wheel is divided into 100 parts consecutively numbered 1 to 100 with each hue assigned a specific number within this range. See *Munsell Book of Colors* (Munsell Color Co., Baltimore, Md., 1942).

22 August 1955

I feel more vexed at impropriety in a scientific laboratory than in a church. The study of nature is intercourse with the Highest Mind.—LOUIS AGASSIZ.

Book Reviews

Weeds. W. C. Muenscher. Macmillan, New York, ed. 2, 1955. 560 pp. Illus. $10.

This new edition describing 571 species, with reference to some 40 other weeds and poisonous plants, presents the most comprehensive survey of the weeds of the northern United States and Canada yet available. It compares with the 225 weeds listed in *Weeds of the North Central States* (Univ. of Illinois, *Agri. Expt. Sta. Circ. 718*, 1954) and the 437 in *Weeds of California* (California Dept. of Agri., Sacramento, 1951). Since no one work exists on the North American weed flora, the total species can only be estimated at somewhat less than 1000.

The leading families with total species are *Compositae* (120), *Gramineae* (65), *Cruciferae* (40), *Leguminosae* (33), with the following genera including the largest number of species: *Polygonum* (15), *Chenopodium* (12), *Cuscuta* (11), *Centaurea* (10), *and Bidens* (7).

The chapters on weed biology are taken verbatim from the 1935 edition, and no new material beyond 1934 is specifically cited. In advancing from weed "chopping" to chemical control, an even greater knowledge is required of the biology and ecology of the individual weed species than ever before. The bibliography of 321 items shows an increase of 41 over earlier printings, and certain chapters list new sources of material, such as the proceedings of the regional weed control conferences and the "Bibliography of weed investigations" published in the journal *Weeds*. As the preface states, little attention has been given to chemical control measures. This is indeed unfortunate, since a wealth of such information has now been accumulated. To have listed the sensitivity of certain weed species to 2,4-D alone would have been most useful. The author has not acknowledged the significance of 20 years' additional experience with biological control.

The newly added weeds include species of *Rumex, Halogeton, Silene, Spergula, Ranunculus, Descurainia, Aegopodium, Ampelamus, Ellisia, Veronica, Linaria, Campsis, Bidens, Cnicus, Eupatorium,* and *Parthenium*. Six new figures illustrating ten of these are included. No reference has been made to the extensive literature on two weeds of current concern, *Halogeton glomeratus,* and giant foxtail (*Setaria faberii*).

Emil Korsmo has stated that in the northern temperate zone the weed flora may constitute 8 to 10 percent of the entire vegetation. When based on species number, the 571 species here listed make up 10 percent of the 5523 species covered in the area of *Gray's Manual* (9th ed.) range. Another example might be cited in the 413 weeds listed for New York State (*Cornell Ext. Bull. 891*), which is 14 percent of the 2876 species included in the state flora. Such an aggressive element of our flora certainly is a constant threat to agriculture and requires that the newest techniques be applied and that better control methods be provided by continued research.

The illustrations are excellent, and many provide some aspect of the weed well enough (for example *Erigeron canadensis*) to enable one to identify it immediately. Should a future edition be prepared, distribution maps and the use of the vertical column for flowering dates (as in Deam's *Flora of Indiana,* Indianapolis, 1940) would greatly enhance the usefulness of the work.

This work with detailed keys for identification and full descriptions still provides our best illustrated guide to the weed flora of an important area of the country.

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Schools of Psychoanalytic Thought. An exposition, critique, and attempt at integration. Ruth L. Munroe. Dryden, New York, 1955. xvi + 670 pp. $7.50.

This book contains the best bird's-eye view of psychoanalytic thought ever written. It presents each school competently and sympathetically. It brings out common factors and differences without the polemical flavor always present when protagonists of one school criticize another. It is sensibly organized around Freud's work but does not spare a critique of Freud along with other thinkers.

But what kind of bird do you have to be in order to get the force of this over-all view? I think you have to be a pretty rare one. Ideally, you should be a psychoanalyst who has a stock of daily-life experiences to attach to the special terms that are used; or, better still, you should be a researcher who has submitted himself seriatim to treatment by a practitioner of each of the schools and has thus acquired the special experiences needed to give meaning to the terms used by each. My general point is that this comparison of theories is not a good introductory book for anyone, does not simplify matters for the layman, and can be unreservedly recommended only to specialists of some one of the several schools. For them it will be a valuable reference work.

Personally I got a good deal out of the book, although taken as a whole it is a terrible dose to be read in a few sittings. I was glad to be reminded of the firm biological and genetic anchorage of Freud's theory, its delicate and powerful sketch of the organ systems of the body as they develop under cultural pressure. I agreed that Freud's system could stand further development in terms of the "self-concept" or Ego theory. Adler's notion of a "life-style" has always been stimulating, but it seems to me, as to Ruth Monroe, that it fails to give an adequate account of childhood. Horney's emphasis on "basic anxiety" is an important organizing concept, and she appears as the expert therapeutic tactician that I knew her to be. Fromm is the social philosopher, grounded in analysis, but more interested in a critique of our way of life than in a theory of personality. Sullivan's idea of the repression of the organized self in schizophrenia still seems of extraordinary value; in some odd way his eyes were unmisted to facts that are blurred for most of us. Jung gave me an emotional thrill this time, as he always does. There is something eerie, poetic, and perceptive about his terms and his theories—but the notion of the "racial unconscious" seems to be refuted by genetic and anthropological fact. The impassioned Rank, with his view of "will" and "counter-will" coiled in eternal struggle, also has something that is important to say about man, but his history of the individual life is beclouded. At the end, after the canvass of theories, one returns to Freud, refreshed but relieved, to see man's struggle pretty much as he sees it.

Munroe does not say (although she ought to) that this whole field should not be viewed as "finished science" but rather as exploratory work looking toward science. There is no mention of observer reliability, validity, correlation, experiment, or reinforcement. There is a sense in which we have no science in this field, because we have no "data"; but recordings of analytic proceedings can now be

made, and for the first time we will have data subject to common scrutiny and evaluation. "In the home" studies of children can also be made, and the exact terms of their emotional and social growth can be described. The trouble with this field is that it is, as one astute friend described it, a "night-school science"—that is, a body of facts and concepts created in practice by hard-worked clinicians who wrote their papers in the evening. This history has its great merits but also its flaws. The field of psychoanalytic researches should be adopted by the university and the research institute, but we had better hurry while the subject matter is still in the public domain of science. What was it that someone said about a fabulous foundation?

JOHN DOLLARD
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Surgical Procedures on the Gastrointestinal Tract of Animals in Preparation for Chronic Experiments. E. N. Speranskaya. Academy of Medical Sciences, U.S.S.R., Moscow, 1952. 64 pp. (in Russian). Illus.

Pavlov's research on gastrointestinal physiology that earned him the Nobel prize in 1904 was based on the concept of the organism as one indivisible homeostatic unit. In order to study normal functions of various digestive glands, Pavlov devised a number of surgical procedures on dogs that made it possible for him to conduct investigations under chronic conditions.

"Acute experiments," wrote Pavlov in 1902, "give a satisfactory answer to a very limited number of problems; in most cases the operated animals differ so markedly from the normal—often in respect to the very function that forms the subject of the investigation—that the latter loses its meaning and becomes fruitless." He therefore devised surgical methods "by means of which one can prepare the animal in such a manner that, after recovering from the after-effects of surgery, it could serve for observations, as faultless as possible, on this or that gland." [Physiological surgery on the digestive tract I. General methodology." *Ergeb. Physiol.* **1**, 1 (1902). Reprinted in Russian in I. P. Pavlov, *Studies on the Physiology of Digestion*. Acad. Med. Sciences, Moscow, U.S.S.R. (1952), pp. 315–316.]

Moreover, Pavlov was convinced that "animals operated according to these methods represent excellent instructional material. For this reason we think that college physiological laboratories need such animals as much as they do the most important physiological equipment."

The booklet contains detailed and succinct descriptions of the surgical techniques devised by Pavlov for his chronic experiments. The numerous line drawings are excellent and should enable any competent physiologist or surgeon to perform the same operations successfully. The author includes instructions on pre- and post-operative care of the animals as well as on the special instruments and equipment required for the procedures.

Among the techniques described are those related to establishing chronic fistulas of the salivary glands, esophagus, stomach, gall bladder, pancreas, and intestine as well as procedures for isolating Pavlov and Savich-Brestkin gastric pouches.

The use of such animal preparations for chronic experiments and observations by students in medical and veterinary courses in physiology and pharmacology might represent a significant step toward the integrative approach to medical education and practice. One can hardly expect students to gain a realistic knowledge of normal physiological processes and of physiological homeostasis by limiting their observations to the reactions of organs isolated from integrative nervous and endocrine influences or by recording responses of animals subjected to anesthetic agents and acute surgical trauma. Observations on unanesthetized animals prepared for chronic experiments may help to bridge the gap between cell and organ physiology and the physiology of the organism as a biological unit.

Such chronic animal preparations should also find useful applications in connection with the screening of drugs used to influence secretions of various digestive glands.

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Reports on Progress in Physics. vol. XVIII. A. C. Stickland, Ed. The Physical Society, London, 1955. £2 10s, nonfellows; 27s. 6d, fellows.

Research results in physics are now being published at a rate of about 1000 papers a month. (*Physics Abstracts* contained 11,693 entries in 1954.) The contributions of the Physical Society toward organization and synthesis of the many discoveries of physicists are continued in this volume. Like its predecessors, volume XVIII contains a group of papers, each one of which is a careful survey of experimental and theoretical findings during the past few years with respect to some aspect of physics.

The opening article, "The displacement of atoms in solids by radiation," by G. H. Kinchin and R. S. Pease, is a discussion of effects of radiation on structure and composition of solids. Quoting from the paper's introductory section, "Much of the current interest in these irradiation effects has been aroused by the need to understand and mitigate them in materials used in nuclear reactors. . . . However, with the increased understanding of the role of defects in crystalline solids, considerable interest has also been aroused by the possibility of the controlled introduction of defects by irradiation, which can have valuable application." Readers will be interested in finding the late H. G. Wells, in the novel *Tono-Bungay* (1909), among the early writers cited on irradiation effects in solids.

In the second article, B. T. Price discusses, in "Ionization by relativistic particles," the theories of "the relativistic increase of energy-loss by ionization and of the density effect" and also the relevant experimental evidence and its comparison with theory. J. L. Symonds contributes a paper on "Methods of measuring strong magnetic fields." In a paper on "Theory of radiation," J. C. Gunn gives a survey discussion of quantum electrodynamics, with some attention also to meson field theory. E. W. Lee writes on "Magnetostriction and magnetomechanical effects." This paper is followed by one on "Electrostriction," by H. F. Kay, in which "Single crystals are . . . discussed . . . in detail. . . . Similarly the more complicated ceramic materials are dealt with."

A survey of "Magnetic cooling" is contributed by E. Ambler and R. P. Hudson. Experimental methods and the properties below 1°K of paramagnetic salts and of other materials are discussed. Also, cascade demagnetizations and continuous cooling cycles and the achievement of spatial orientation of atomic nuclei by magnetic cooling are described. The paper, "Paramagnetic resonance II," by K. D. Bowers and J. Owen, is complementary to one in volume XVI by B. Bleaney and K. W. H. Stevens. Paramagnetic resonance data are collected in the paper for "crystalline solids containing ions of the transition groups, and those parts of the theory necessary for an understanding of the results are presented in a fairly simple way." J. D. Craggs and C. A. McDowell write on "The ionization and dissociation of complex molecules by electron impact."

In the final paper of the volume, entitled "A survey of field theory," a group of lectures given at the University of Birmingham in December 1954 are now published. The names of the lecturers, R. E. Peierls, A. Salam, P. T. Matthews, and G. Feldman, speak for the authoritativeness of the paper. The survey is intended for the "non-specialist," and although it therefore is not as detailed in

treatment of its subject topic as papers usually are in this series of volumes, it should be of interest and value to a wide group of experimental and theoretical physicists.

Individual articles in this volume of reports may be purchased from the Physical Society, London.

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Fifth Symposium (International) on Combustion. Combustion in engines and combustion kinetics. Standing Committee on Combustion Symposia of the Combustion Institute. Reinhold, New York; Chapman & Hall, London, 1955. xxvi + 802 pp. Illus. $15.

The fifth symposium, held at the University of Pittsburgh, primarily emphasized the chemical aspects of combustion, especially combustion kinetics. By means of a series of invited papers, it did take cognizance of the role of combustion in the development and design of engines. Six invited papers were on the unsolved problems of engine combustion in internal-combustion engines, diesel engines, liquid-fuel rocket engines, ramjets, turbojets and solid-propellant engines. This series of six papers is a reminder that there are still objectionable odors from diesel engines, combustion instability in rockets, extremely poor combustion efficiency in ramjets, and other serious unsolved problems. Five invited papers were on combustion kinetics. These included a thought-provoking paper on high-temperature reaction systems, two papers on kinetics of hydrocarbon combustion, and two papers on space requirements for combustion.

In addition to the 11 invited papers, this volume contains the text and discussions of 90 papers delivered at the symposium. Six of the papers are on the combustion of fuel droplets. The preheat and vaporization stages, the effect of turbulence, ignition lag, fuel droplet size, mass burning rate, flame velocity, flammability limits, and flame stability, from the theoretical and experimental viewpoint, are contained in this set of papers. Nine of the papers discuss the various aspects of propellant burning such as monopropellant and bipropellant systems, ignition lags and hyperbolic fluid burning rates. Six papers treat the combustion of solids, such as carbon particles, pulverized coal, magnesium ribbon, and pyrotechnics. The experimental techniques used for the study of the kinetics of solid-phase reactions are interesting. Diffusion flames and carbon formation are discussed in five of the papers. Studies of cool flames, auto ignition, and high-turbulence combustion chambers are reported on in eight of the papers on combustion in engines.

Especially interesting are five papers on special techniques that include a new shock tube for studying high-temperature gas phase reactions, use of Langmuir probes for ionization studies of flames, polarographic studies of cool flames, microwave studies of ionization, and the use of iodine absorption spectrum for temperature measurements.

The many facets of the kinetics of combustion reactions are discussed in a total of 45 papers. Of these approximately half are concerned with the combustion of hydrocarbons. Progress is being made in correlating the reactivity of complex hydrocarbon molecules with the process of energy transfer among the bonds within the molecule. Of the final set of papers, five are concerned with flame spectra and one with the dissociation energy of the OH radical. The volume is completed with résumés of two panel discussions, one on heterogeneous burning and the other on the status of the theory of the kinetics of combustion reactions.

This book should be stimulating to research workers, engineers, and scientists who are active in the combustion field. Although much experimental work is being done, new experimental techniques seem to be required to provide the information needed to confirm the present theoretically developed concepts of the kinetics of combustion processes.

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Miscellaneous Publications

(Inquiries concerning these publications should be addressed, not to Science, *but to the publisher or agency sponsoring the publication.)*

Survey on Vibration and Shock Isolation. National Standards Laboratory Tech. Paper No. 7. J. A. Macinante. Commonwealth Scientific and Industrial Research Organization, Melbourne, Australia, 1955. 42 pp.

The Use of Nuclides in the Determination of Organic Reaction Mechanisms. Peter C. Reilly Lectures in Chemistry, vol. XI. Lars C. S. Melander. University of Notre Dame Press, Notre Dame, Ind., 1955. 96 pp. $3.

Hospitals Served by the Red Cross Blood Program and Usage of Blood and Derivatives Distributed 1954–55. American National Red Cross, Washington, D.C., 1955. 56 pp.

Centrale Organisatie T.N.O. Jaarverslag 1954. Central Organization for Applied Scientific Research, Koningskade 12, The Hague, Netherlands, 1955. 353 pp.

Social Science Research Council, Annual Report 1954–1955. The Council, New York 17. 86 pp.

The Safety of Artificial Sweeteners for Use in Foods. A report by the Food Protection Committee of the Food and Nutrition Board. National Academy of Sciences–National Research Council, Washington, 1955. 10 pp.

Clearing the Main Channels. Thirty-fifth annual report of the American Civil Liberties Union. 1 July 1954 to 30 June 1955. American Civil Liberties Union, New York 10, 144 pp. $0.50.

The Papyrus Swamps of Uganda. G. S. Carter. Heffer, Cambridge, England, 1955. 25 pp.

Joint FAO/WHO Expert Committee on Meat Hygiene, First Report. WHO Technical Rept. Ser., No. 99. World Health Organization, Geneva, 1955. 52 pp. $0.60.

The Economics of Feed Materials and Fuel Processing Problems. J. Carlton Ward, Jr. Vitro Corp. of America, New York 16, 1955. 22 pp. Free.

Nuclear Level Schemes. A = 40 – A = 92 (Covering the Elements Ca – Zr). A collection of diagrams showing positions and properties of nuclear energy levels, characteristics of radioactive decay and nuclear reactions, together with a tabular compilation of the experimental data and bibliographic references to the original papers. K. Way, R. W. King, C. L. McGinnis, and R. van Lieshout. Nuclear Data Project, National Academy of Sciences–National Research Council, Washington, 1955 (Order from Supt. of Documents, GPO, Washington 25). 221 pp. $1.75.

Proceedings of the Conference on Effects of Radiation on Dielectric Materials. ONR Symposium Report ACR-2. Held at Naval Research Laboratory, Washington, D.C., 14–15 December 1954, under the joint sponsorship of Naval Research Laboratory and Office of Scientific Research, Air Research and Development Command. Office of Naval Research, Washington, 1955 (Order from Office of Technical Services, Dept. of Commerce, Washington). 169 pp. $4.25.

A Check-List of the Fossil and Prehistoric Birds of North America and the West Indies. Misc. Collections, vol. 131, No. 5. Alexander Wetmore. Smithsonian Institution, Washington, 1956. 105 pp.

Contributions to the Nomenclature, Systematics, and Morphology of the Octocorallia. Proceedings of the U.S. National Museum, vol. 105, No. 3357. Frederick M. Bayer. Smithsonian Institution, Washington, 1955. 14 pp.

Recherches sur les Concomitants Electrencéphalographiques Eventuels du Papillotement et de la Fusion en Lumière Intermittente. J. Rutchmann. *Archives de Psychologie,* Geneva, 1955. 100 pp.

Our Natural Resources–and Their Conservation. Pamphlet No. 230. Richard L. Neuberger. Public Affairs Committee, New York, 1956. 28 pp. $0.25.

How to Write Technical Reports and Still Maintain Your Sanity. A. D. Ehrenfried. Technical Marketing Associates, Concord, Mass. 8 pp. $0.25.

Precooked Frozen Foods, a Symposium. Advisory Board on Quartermaster Research and Development. Quartermaster Food and Container Institute for the Armed Forces, Chicago 9, 1955. 76 pp.

Scientific Meetings

Role of Council for International Organizations in Medical Sciences

The Council for International Organizations in the Medical Sciences is now 6 years old and has demonstrated its usefulness in a difficult area of essential activity. Scientific organizations are obviously useful to scientists or they would not continue to exist and flourish. However, there are more obvious, more direct, and more personal services performed by societies covering a single discipline in a single country or region than is the case with interdisciplinary and international organizations. Nevertheless, there are strong reasons for maintaining and promoting nongovernmental activities in science at interdisciplinary and international levels.

Many serious students of science believe that the fragmentation owing to specialization and the increments in volume of publication threaten to throttle advancement of basic knowledge. With more than 50,000 journals of primary publication and more than 1 million papers per year in the whole area of natural science, the problem of identification of information has become impossible to accomplish on an individual basis. In one area, physiology, it has been calculated that in the year 1900 a scholar could scan everything published in that year in 91 days of 8 hours, reading at the rate of 2 minutes per page, but that the volume published in 1950 would require about 5 years to scan in the same way.

One needs no further information to understand why the age of the nonspecialist is past. Every scientist must obviously limit his systematic reading of original literature to subspecialties. It is primarily for reasons related to these facts that abstracting and indexing journals, annual reviews, summarizing literature, and the like are indispensable to science and scientists. Likewise, the special services of seminars, symposia, summarizing lectures, and discussions become more pertinent to the ongoing of science.

CIOMS, at its third assembly, held in Paris, 30 Sept. and 1 Oct. 1955, had the task of formulating a program for international, interdisciplinary work for the next period and preparing a budget to present to WHO and UNESCO, its major financial supporting agencies, to aid scientists in medicine to improve communications. Obviously we must do what we can with existing tools, but we should also attempt to improve our tools. We should eliminate duplication in abstracting, indexing, and reviewing wherever possible, because, for example, a half-dozen incomplete and inadequate abstracting services could, if they cooperated, give substantially complete coverage at no extra cost to anyone. CIOMS is in a strategic position to promote such integration of effort. The only force it has is persuasion, because it is made up of private nongovernmental organizations. It has no vested interests and no national pride. It is interested in getting jobs done effectively for medical science and its application to the welfare of man. It can be altruistic because it has no other justification for existence.

CIOMS is in some danger of losing the support of its sponsors because it does not have as wide organizational support in various countries as it should if it is to function effectively. Most scientists are greatly preoccupied with their immediate research problems and service functions. They rarely take the time or trouble to concern themselves with thought and action about the mechanisms that are essential to the long-time promotion of science. They take journals of primary and of secondary publication for granted. They appear to assume that seminars, symposia, and general lectures "just happen," and that their thought and effort are not needed for improvement or even for continuance.

It is undoubtedly true that voluntary international cooperation is difficult and that it has frequently been frustrating. But as our world shrinks in effective time and space, and as we approach greater interdependence, and particularly as science becomes a world enterprise, such cooperation becomes imperative. We must be willing to devote some of our time and energies to planning and executing cooperative ventures. The world interest in the development and extension of medical knowledge and its utilization should encourage us in our efforts in this organization. CIOMS is the first world-wide interdisciplinary organization in the medical sciences ever to be established. It was born out of the optimism of the late 1940's, but if it should collapse it will take even more optimism to begin another such unusual venture.

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Biological Abstracts

Biological Abstracts, an abstracting and indexing service of the world's biological literature, celebrated its 30th anniversary on 17 Feb. with a scientific symposium at the University of Pennsylvania. Participants in the symposium included David R. Goddard, professor of botany at Pennsylvania; G. Miles Conrad, director of Biological Abstracts; and D. H. Wenrich, professor emeritus of zoology at Pennsylvania. At a dinner meeting, guests were greeted by Gaylord P. Harnwell, president of the university. His welcome was followed by addresses by Ralph E. Cleland, professor of botany at the University of Indiana, and Maurice B. Visscher, professor of physiology at the University of Minnesota.

Although it is an independent organization, Biological Abstracts has been housed at the University of Pennsylvania since it was established in 1926 under a grant from the Rockefeller Foundation. Thus far it has published abstracts of more than 750,000 original articles on research in the medical sciences, agriculture, food technology, and other fields related to the study of animal and plant life.

Meeting Notes

■ A conference on the need for high-school physics was held 27–28 Jan. in Pittsburgh, Pa., under the joint sponsorship of the University of Pittsburgh and the National Academy of Sciences–National Research Council. Participants included representatives from university physics departments, science teachers and supervisors from secondary schools, school superintendents and principals, and representatives from industry and labor in the Pittsburgh area. Recommendations from the conference will soon be published and may be obtained by writing to Prof. W. G. Kelly, Department of Physics, University of Pittsburgh.

■ The AAAS Science Teaching Improvement Program will sponsor a regional conference of scientists to be held on the downtown campus of Northwestern University on 9 Mar. The purpose

of the meeting is to provide an opportunity for university and college scientists to discuss science teacher education programs and relations with secondary schools. All staff members in science and mathematics in colleges and universities in Minnesota, Iowa, Illinois, Wisconsin, and Indiana are cordially invited to attend.

Invitations are being sent to the presidents of the colleges in these states, suggesting that members of science departments be named as representatives of their institutions. Members of the advisory committee for the conference are J. W. Buchta, physics (Minn.); S. S. Cairns, mathematics (Ill.); Ralph E. Cleland, botany (Ind.); Farrington Daniels, chemistry (Wis.); and Emil Witschi, zoology (State University of Iowa).

■ An attendance of 45,000 engineers and scientists is expected for the national convention of the Institute of Radio Engineers that is to be held on 19–22 Mar. in New York. The program includes 55 technical sessions and 714 engineering exhibits. Sessions are scheduled for all four days at the Waldorf-Astoria Hotel, the Kingsbridge Armory, and the Belmont Plaza Hotel.

The program will be highlighted by two special symposia on "The U.S. earth satellite program" and "Color television tape recording." The remainder of the program will cover a wide variety of topics, such as the "Impact of computers on science and society," "Nuclear effects on communication systems," "The future of medical electronics," and "Air traffic control."

■ A conference on communication of information by workers studying sounds of biological significance will be held at Pennsylvania State University 16–19 Apr. Great interest in auditory communication among animals has arisen in recent years. The development of tape recording has made possible simple field and laboratory recording at small expense. Much published information is beginning to appear, but unfortunately, printed words cannot adequately describe bird songs, insect sounds, underwater noises, or the ultrasonic sounds such as those of bats.

The purpose of this conference is to discuss acceptable procedures for recording sounds produced by animals, so that an international collection of these sounds can be established. This would be a collection of sounds whose effects on animal behavior have been determined by field or laboratory observations, not merely a collection of animal sounds, the biological significance of which is unknown or hypothetical.

The conference is viewed as a starting point, not as a conventional symposium for the sharing of information already at hand. The speakers for the first day of the conference will be Donald Griffin, Harvard University; R.-G. Busnel, Laboratoire de Physiologie Acoustique (France); F. Mohres, Universität Tübingen (Germany); and R. J. Pumphrey, University of Liverpool (England).

The remaining days will be given over to informal consideration of recording techniques and standards. Persons who are interested, whether or not they expect to attend, are requested to submit in advance to the committee or to a person who will attend topics that they would like to have discussed.

The planning committee consists of Hubert Frings, Mable Frings, H. K. Schilling, Bertil G. Anderson, and A. Anthony, all of Pennsylvania State University; Donald Griffin of Harvard University; William Schevill of the Woods Hole Oceanographic Institution; and T. C. Schneirla of the American Museum of Natural History.

Society Elections

■ Interamerican Society of Psychology: pres., Otto Klineberg, Columbia University; v. pres., Guillermo Davila, National University of Mexico; sec. general, Werner Wolff, Bard College; treas., Gustave M. Gilbert, Michigan State University.

■ Institute of Radio Engineers: pres., A. V. Loughren, Hazeltine Corporation, 59-25 Little Neck Parkway, Little Neck 62, N.Y.; senior past pres., W. R. Hewlett, Hewlett-Packard Company, Palo Alto, Calif.; junior past pres., J. D. Ryder, Michigan State University; v. pres., Herre Rinia, Philips Research Laboratories, Kastanjelaan, Eindhoven, Netherlands; sec., Haraden Pratt, 1216 Hope St., Springdale, Conn.; treas., W. R. G. Baker, General Electric Company, Syracuse, N.Y. Representative to the AAAS Council is John C. Jensen.

■ American Medical Writers' Association: pres., Richard M. Hewitt, Mayo Clinic, Rochester, Minn.; pres.-elect, Dean F. Smiley, Chicago; past pres., Lee D. van Antwerp, Chicago; 1st v. pres., Russell L. Cecil, New York; 2nd v. pres., Austin Smith, Chicago; sec.-treas. and representative to the AAAS Council, Harold Swanberg, 510 Maine St., Quincy, Ill.

■ Torrey Botanical Club: pres., Lela V. Barton, Boyce Thompson Institute; 1st v. pres., Edwin T. Moul; 2nd v. pres., David D. Keck; cor. sec., Eleanor Witkus, Fordham University; rec. sec., Frank G. Lier; treas., Gily E. Bard. Representatives to the AAAS Council are A. E. Hitchcock and Lindsay S. Olive.

■ American Institute of Chemical Engineers: pres., Walter Gordon Whitman, Massachusetts Institute of Technology; v. pres., J. Henry Rushton, Purdue University; treas., George Granger Brown, University of Michigan; exec. sec., F. J. Van Antwerpen.

Forthcoming Events

March

24–25. American Psychosomatic Soc., 13th annual, Boston, Mass. (T. Lidz, APS, 551 Madison Ave., New York 22.)

24–31. Perspectives in Marine Biology, La Jolla, Calif. (A. A. Buzzati-Traverso, Scripps Institution of Oceanography, La Jolla.)

25–28. American Assoc. of Dental Schools, annual, St. Louis, Mo. (M. W. McCrea, 42 S. Greene St., Baltimore 1, Md.)

25–29. American College Personnel Assoc., Washington, D.C. (Miss C. M. Northrup, Univ. of Denver, Denver, Colo.)

28–3. Colloquium on Frontiers in Physical Optics, Boston, Mass. (S. S. Ballard, Visibility Laboratory, Scripps Institution of Oceanography, San Diego 52, Calif.)

29–31. Alpha Epsilon Delta, 11th national convention, Jackson, Miss. (M. L. Moore, 7 Brookside Circle, Bronxville 8, N.Y.)

29–31. Pennsylvania Acad. of Science, Indiana. (K. Dearolf, Public Museum and Art Gallery, Reading, Pa.)

29–31. Southern Soc. for Philosophy and Psychology, Asheville, N.C. (J. E. Moore, Georgia Inst. of Technology, Atlanta.)

29–31. Symposium on Fundamental Cancer Research, 10th annual, Houston, Tex. (G. Taylor, Univ. of Texas Postgraduate School of Medicine, Houston 25.)

30–31. Alabama Acad. of Science, annual, Montevallo. (H. A. McCullough, Howard College, Birmingham, Ala.)

April

2–5. Assoc. of American Geographers, annual, Montreal, Canada. (B. W. Adkinson, Library of Congress, Washington 25.)

2–7. Symposium on Crystallography, Madrid, Spain. (M. Abbad, Serrano 118, Madrid.)

3. Microcirculatory Conf., 3rd, Milwaukee, Wis. (G. P. Fulton, Dept. of Biology, Boston Univ., 675 Commonwealth Ave., Boston 15, Mass.)

3–4. Tissue Culture Assoc., 7th annual, Milwaukee, Wis. (D. C. Hetherington, Duke Univ. School of Medicine, Durham, N.C.)

3–9. International Symposium on Macromolecular Chemistry, Rehovoth, Jerusalem, and Haifa, Israel. (A. Katchalsky, Weizmann Inst. of Science, Rehovoth.)

4–6. American Assoc. of Anatomists, annual, Milwaukee, Wis. (N. L. Hoerr, 2109 Adelbert Rd., Cleveland 6, Ohio.)

4–6. American Soc. of Lubrication Engineers, 11th annual, Pittsburgh, Pa. (Administrative Secretary, ASLE, 84 E. Randolph St., Chicago 1, Ill.)

4–7. International Cong. of Medical Radiography 2nd, Paris, France. (Secretariat, 66, Boulevard St. Michel, Paris 6.)

5–6. Conf. on Magnetic Amplifiers, Syracuse, N.Y. (C. A. Priest, 314 Hurlburt Rd., Syracuse 3.)

5–7. Optical Soc. of America, Philadelphia, Pa. (A. C. Hardy, Room 8-203, Massachusetts Inst. of Technology, Cambridge 39.)

6–7. American Assoc. of University Professors, St. Louis, Mo. (R. F. Fuchs, AAUP, 1785 Massachusetts Ave., NW, Washington 6.)

6–7. National Speleological Soc., Nashville, Tenn. (Mrs. L. Cutler, 2829 Buchanan St., Arlington 6, Va.)

6–8. American Assoc. of Physical Anthropologists, Chicago, Ill. (J. L. Angel, Daniel Baugh Institute of Anatomy, Jefferson Medical College, Philadelphia 7, Pa.)

7–8. American Soc. of Hospital Pharmacists, Detroit, Mich. (Miss G. Niemeyer, 2215 Constitution Ave., NW, Washington 7.)

7–10. National Assoc. of Boards of Pharmacy, annual, Detroit, Mich. (P. H. Costello, NABP, 77 W. Washington St., Chicago 2, Ill.)

8. American College of Apothecaries, Detroit, Mich. (R. E. Abrams, Hamilton Court, Philadelphia 4, Pa.)

8–10. American Assoc. of Colleges of Pharmacy, Detroit, Mich. (R. A. Deno, College of Pharmacy, Univ. of Michigan, Ann Arbor.)

8–13. American Chemical Soc., Dallas, Tex. (A. H. Emery, ACS, 1155 16 St., NW, Washington 6.)

8–13. American Pharmaceutical Assoc., annual, Detroit, Mich. (R. P. Fischelis, APA, 2215 Constitution Ave., NW, Washington 7.)

8–13. Symposium on Problems of Automation, Milan, Italy. (Consiglio Nazionale delle Ricerche, Ufficio Congressi e Mostre, 7 Piazzale delle Scienze, Rome, Italy.)

9–11. American Assoc. of Feed Microscopists, annual, Terre Haute, Ind. (R. C. Wornick, Agricultural Research Dept., Chas. Pfizer & Co., Inc., Terre Haute.)

9–12. International Anesthesia Research Soc., 30th annual cong., Miami Beach, Fla. (R. J. Whiteacre, 13951 Terrace Rd., Cleveland 12, Ohio.)

10–11. Symposium for Management on Applications of Analog Computers, Kansas City, Mo. (O. Fanning, Midwest Research Inst., 425 Volker Blvd., Kansas City 10.)

12. Assoc. of Vitamin Chemists, Chicago, Ill. (M. Freed, Dawes Products, 4800 S. Richmond, Chicago 32.)

13–14. Louisiana Acad. of Science, annual, New Orleans, La. (H. B. Boudreaux, Dept. of Zoology, Louisiana State Univ., Baton Rouge 3.)

14. South Carolina Acad. of Science, annual, Clemson, S.C. (H. W. Freeman, Univ. of South Carolina, Columbia.)

15–16. American Soc. for Artificial Internal Organs, Atlantic City, N.J. (P. F. Salisbury, Cedars of Lebanon Hospital, 4751 Fountain Ave., Los Angeles 29, Calif.)

(See issue of 17 February for comprehensive list)

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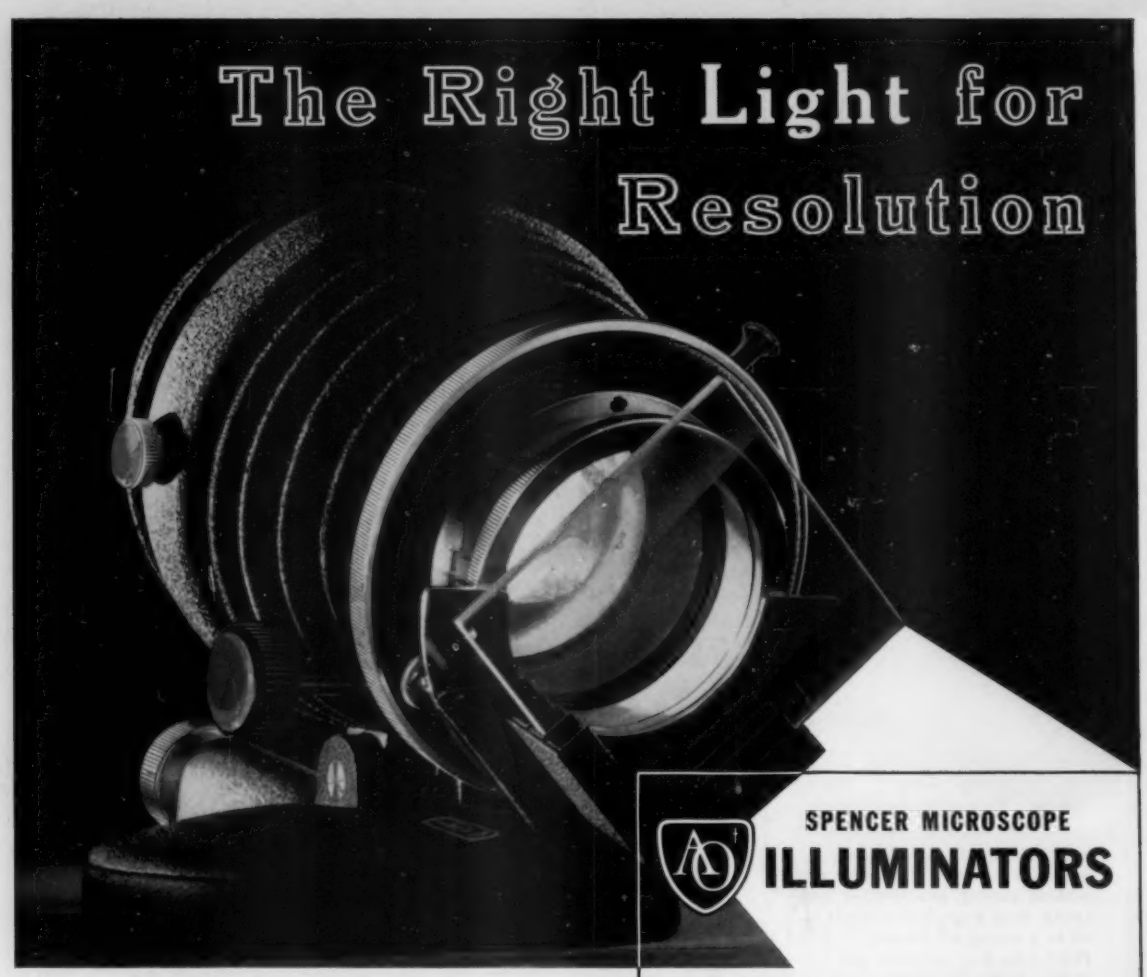

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